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APRIL, 1922

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INDICATIONS FOR THE REMOVAL OF THE SPLEEN IN INFANTS AND CHILDREN*

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Hemolytic jaundice, Banti's disease, Gaucher's disease and von Jaksch's anemia, are four names given to pathologic processes for the relief or cure of which removal of the spleen may be the only treatment.

Hemolytic jaundice, in the yellowness of the skin and sclera, presents an outward and visible sign which gives obvious aid in the determination of a diagnosis.

Banti's disease and Gaucher's disease have no distinguishing symptoms and physical signs by which they can be identified clearly. It is impossible in the early stages, and difficult even in the later stages, to give a name to the pathologic process representing these diseases, and it is just in the early stage of Banti's or Gaucher's disease that splenectomy is of greatest value.

Von Jaksch's disease is at present sub judice, being regarded by some as not a distinct entity. Figures 1, 2 and 3 are the microphotographs of a spleen of Banti's disease and Figures 4 and 5 of a spleen of Von Jaksch's disease. A comparison of these two sets of pictures would justify the statement that they might be two stages of the same pathologic process.

In view of the difficulty of giving a name (Banti's disease; Gaucher's disease) to certain symptom complexes in which anemia and a large spleen are the prominent manifestations, and for which splenectomy may be the only proper treatment, it is necessary to have certain criteria for the removal of the spleen. These criteria will be brought out in the analysis of the two cases of Banti's disease and one of Gaucher's disease which are reported in this paper. They were treated by splenectomy.

An attempt has been made to collect the reports of all previous splenectomies in children under 14 years of age. Table 1 contains this information. No doubt some reports have been missed in the search. Information about splenectomies not recorded in this table would be appreciated, as a complete record is desired. The table represents a total of fifty-one splenectomies which are distributed as follows: von Jaksch's disease, 5; splenic anemia and Banti's disease, 20; Gaucher's

* Received for publication Dec. 23, 1921.

TABLE 1.—Summary of Splenectomies Done on Children Under 14 Years of Age

Diagnosis	Author	Age and Sex	Spleen	Blood Examination	Result	Remarks
1. von Jaksch's anemia	Pool, E. H.: Ann. Surg. **61**: 349, 1915	8 mos. Male	6.5 cm. below costal margin; 10×7×4 cm.; Wt., 3½ oz.; malpighian bodies few, small and indistinct; myeloidzation of pulp	Before splenectomy: R.B.C. 1,400,000 to 2,400,000; Hb. 30-45%; E. 2%; L. 49%; W.B.C. 17,000-54,000; P. 35%; T. 3%; L.M. 1%; Myel. 5%; nucleated reds 6-66 per 100 W.B.C.; megaloblasts. After: 4,000,000; Hb. 85%; nucleated reds 131 per 100 W.B.C.	Died of bronchopneumonia 2 mos. after discharge	
2. von Jaksch's anemia	Stillman, R. G.: Am. J. M. Sc. **153**: 218, 1917	9 yrs. Female	15 cm. below costal margin; Wt., 1.420 gm.; vascular increase connective tissue; follicles small, indistinct; sinuses filled with large undifferentiated mononuclear cells; pulp contains myelocytes; monoblasts, R.B.C.	Before splenectomy: R.B.C. 2,400,000; Hb. 25%; W.B.C. 15,000; P. 40%; nucleated red cells. After 23 mos.: R.B.C. 4,600,000; Hb. 65%; W.B.C. 19,200; P. 31%; nucleated reds	6 yrs. after operation: Hb. about 60%; much improved (Stillman's personal communication)	Spleen large since 2 yrs. of age; case regarded by Krumbhaar as possible hemolytic jaundice
3. von Jaksch's anemia	Ibid	18 mos. Female	Edge 6.5 cm. below costal margin; Wt., 227 gm.; 14½×9¼×3½ cm.; malpighian bodies about normal in size, numerous; trabecula indistinct; pulp more cellular than normal, contains many monoblasts, R.B.C. and myelocytes	Before splenectomy: R.B.C. 2,700,000; Hb. 45%; W.B.C. 12,000; P. 47%; 12 nucleated cells to 100 W.B.C.; poikilocytosis aniscytosis, polychromatophilic. After 8 months: R.B.C. 5,700,000; Hb. 67%; W.B.C. 21,900; P. 36%	3 yrs. after operation perfectly well; blood picture practically same as after 8 months	Premature 7 mos.; Wassermann negative
4. von Jaksch's anemia	Thursfield, H. D., Gow, A. E.: Splenomegaly and splenectomy, St. Bartholomew's Hosp. Rep. **50**: 59, 1914	17 mos. Male	Spleen to symphysis and mid line; Wt., 500 gm.; thickening of trabecula; pulp infiltrated in the cells resembling myelocytes	Before splenectomy: R.B.C. 467,000; Hb. 40%; W.B.C. 37,800; normoblasts and megaloblasts. After: 9½ yrs.; R.B.C. 5,000,000; W.B.C. 6,200; morphologically normal	Cured; 3 yrs. after splenectomy, healthy	Case originally reported by Wolf, H.: Berl. klin. Wchnschr. **63**: 1565, 1906
5. von Jaksch's anemia	French, H., and Turner, P.: Case of Splenic Anemia Treated by Splenectomy, Proc. Roy. Soc. Med. **7**: Clin. Sec. 77, 1913-14	5 yrs. Male	Spleen enlarged at 6 months before operation; Wt., 18 oz.; 7×5 inches	Before splenectomy: R.B.C. 1,900,000; Hb. 20%; W.B.C. 21,000. After: Hb. 85%	17 mos. after operation is rosy-cheeked normal boy, attending school, apparently cured	Wassermann positive
1. Splenic anemia (Banti's disease)	Amesse, J. W.: Splenic Anemia in Children, Colorado Med. **17**: 12, 1920	6 yrs.	Weight about 2 lbs.; 17×7×7	Before splenectomy: R.B.C. 1,300,000; Hb. 30%; W.B.C. 5,300. After 3 mos.: R.B.C. 5,200,000; Hb. 80%; W.B.C. 13,000; P. 47%; S.L. 38%	1½ yrs. after splenectomy: patient goes to school and enters into general games; gained 20 lbs.; eats well and sleeps well	Anemia since 3 yrs. old
2. Banti's disease	Gaston, J. M.: Two Splenectomies, Their Lessons, Internat. Clin., ser. 30, **1**: 194, 1920	14 yrs. Male	Enlarged to navel; Wt., 3 lbs.	Before splenectomy: Hb. 80%.....	8 mos. after operation: has gained in weight and was in good health	
3. Splenic anemia (Banti's disease)	Fowler, R. S.: Splenectomy for Splenic Anemia, N. Y. State J. M. **14**: 435, 1914	14 mos. Female	No history of enlarged spleen; Wt., 150 gm.; splenic pulp firmer than normal; microscopically typical of splenic anemia; distinct increase of fibrous tissue	Before splenectomy: R.B.C. 3,316,000; Hb. 50%; W.B.C. 30,000; P. 40%; L.M. 12%; S.M 38%; many normoblasts; occasional megaloblasts; anisocytosis; achromia. After 1 mo.: R.B.C. 3,430,000; Hb. 65%; W.B.C. 15,000; P. 20%; S.M. 78%; T. 2%; polychromesica; anisocytosis; monoblasts; megaloblasts	1 month after operation much improved	
4. Splenic anemia	Fowler: Ibid	5½ yrs. Sex ?	.....	Anemia more marked than in above case	After leaving hospital child died of recurrence of intestinal hemorrhages	No further details in the report

		Sex ?			recurrence of intestinal hemorrhages	

5.	Splenic anemia (Banti's)	Giffin, H. Z.: Splenectomy for Splenic Anemia in Childhood, Ann. Surg. **62**: 679, 1915	2½ yrs. Female	No history of enlargement: Wt., 100 gm.; moderately diffuse fibrosis; hypertrophy of reticula-endothelium of the sinuses	Before splenectomy: R.B.C. 2,010,000; Hb. 20%; W.B.C. 4,000; P. 22%; S.L. 50%; E. 2.3%; L.L 12.3%; Bas. 2.3; Neut. myelocytes 3%; 1 normoblast to 300 cells; R.B.C. showed anisocytosis and moderate polychromatophilia. After 3 days: Hb. 27%; W.B.C. 14,600; P. 71.3%; normoblasts 76 to 300 W.B.C.	Not stated	
6.	Banti's disease	Sherren, James: Surgical Treatment of Certain Diseases by Splenectomy. Ann. Surg. **68**: 379, 1918	12 yrs. Male	Spleen enlarged; Wt., 18 oz.; fibrosis of reticulum of pulp; hemorrhage and slight deposit of iron frequent in and around adventitia of vessels close to malpighian bodies	Before splenectomy. R.B.C. 4,300,000; Hb. 75%; W.B.C. 2,300; P. 54%; E. 2%; S.L. 20%; L.L. 20%; L. hyalin cells 4%. After 1 mo.: R.B.C. 4,800,000; Hb. 80%; W.B.C. 5,000; P. 75%; E. 2.5%; S.L. 5%; L.L. 8.5%; L. hyalin cells 8.5%; T.O. 5%	4 yrs. after operation in perfect health	In same article Sherren mentions a splenectomy in a boy 14 yrs. with advanced cirrhosis of the liver; death 48 hrs. after operation; no further details
7.	Splenic anemia (Banti's)	Knott, v. B.: Splenic anemia in a 5 Years' Old Boy, J. A. M. A. **52**: 963, 1909	5 yrs. Male	Enlargement of spleen noticed same year; Wt., 500 gm.; 17.1×9×4 cm.; increase of connective tissue throughout	Before splenectomy: R.B.C. 1,762,000; Hb. 32%; W.B.C. 5,890; P. 78%; L.L. 4%; S.L. 17%; myelocytes 1%. After 1 mo.: R.B.C. 4,240,000; Hb. 82%; W.B.C. 4,250; S.L. 28%; myelocytes 1%	Improvement soon after operation marked	
8.	Splenic anemia (Banti's)	Hall, F. de Haviland, and Spencer, W. S.: Splenectomy for Splenic Anemia, Proc. Roy. Soc. Med. **2**: Clin. Sec. 238, 1909	8½ yrs. Female	No history of enlargement of spleen; Wt., 2¾ lbs.; spleen showed nothing abnormal except enlargement of vessels with blood	Before splenectomy: R.B.C. 4,060,000; Hb. 65%; W.B.C. 1,200; P. 28%; L. 72%. After 1½ mos.: R.B.C. 4,650,000; Hb. 62%; W.B.C. 12,600; P. 40%; L. 15%	2 mos. after operation patient reports good appetite, though showing slight anemia	
9.	Banti's disease	D'Espine, A.: La Maladie de Banticheæ L'Enfant, Rev. méd. d. l. Suisse **33**: 356, 1913	15½ mos. Female	Wt., 201 gm.; 11×7×3.5; spleen showed hyperplasia with diffuse fibrosis and excess of the myeloid elements	Before splenectomy: R.B.C. 3,700,000; Hb. 45%; W.B.C. 13,640; P. 52%; L. 35%; T. 4%; L.M. 8%; E. 1%; normoblasts few. After 1 mo.: R.B.C. 2,660,000; Hb. 50%; W.B.C. 33,720; P. 31%; L. 43%; T. 7%; L.M. 18%; E. O. 5%	Child improved after operation, but died 5 weeks after of bronchopneumonia	
10.	Splenic anemia	Sargent, P.: Case of Splenic Anemia Treated by Splenectomy, Proc. Roy. Soc. Med. **7**: Clin. Sec. 76, 1913-14	10 yrs. Female	Edge of spleen palpable on admission	Before splenectomy: R.B.C. 4,300,000; Hb. 40%; W.B.C. 2,000; P. 63%; S.L. 33%; L.L. 3%; fair number of normoblasts; moderate poikilocytosis. After 13 mos.: R.B.C. normal; no normoblasts; P. 35%; S.L. 58.5%; L.L. 1.5%	One year after operation fairly good health	November, 1912, abdomen began to enlarge
11.	Splenic anemia (Banti's)	Hoffman, G.: Case of Splenic Anemia Treated by Splenectomy, Proc. Roy. Soc. Med. **7**: Clin. Sec. 78, 1913-14	12 yrs. Female	Spleen projected 2½ in. below costal margin, 21 mos. before operation; perisplenitis and cirrhosis	Before splenectomy: R.B.C. 4,400,000; Hb. 90%; W.B.C. 3,060. After 3 yrs. and 10 mos.: R.B.C. 5,475,000; Hb. 100%	In good health; no hemorrhages 3 yrs. 10 mos. after operation	R.B.C. had previously been as low as 2,200,000
12.	Banti's disease	Grützner: Beitrag zur Lehre vom Morbus Banti, Beitr. z. klin. Chir. **85**: 131, 1913	10 yrs. Female	No history of enlarged spleen; Wt., 450 gm.; 19×12×4.5 cm.: capsule and trabecula made up of thick bluish fibers; similar fibers through entire reticulum; lymphocytes in pulp diminished	Before splenectomy: R.B.C. 2,400,000; Hb. 20%; W.B.C. 2,700; P. 64%; L. 32.5%; E.O. 5%; normoblasts and transitionals 3%; poikilocytosis; slight anisocytosis. After 4 weeks: R.B.C. 3,500,000; Hb. 80%; W.B.C. normal	Immediate improvement after operation; no late results stated	
13.	Splenic anemia (Banti's)	Hutchinson, J.: Excision of the Spleen for Splenic Anemia, Proc. Roy. Soc. Med. **6**: Surg. Sec. 236, 1912-13	11 yrs. Male	Spleen enlarged and tender 4 yrs. previously; spleen showed firm hypertrophy of the whole organ without signs of inflammation	Before splenectomy, 1 mo.: R.B.C. 2,100,000; Hb. 30%; W.B.C. 3,800; P. 63.5%; S.L. 23.5%. After 2 mos.: R.B.C. 5,000,000; Hb. 65%; W.B.C. 9,400	One year after operation in excellent health	

TABLE 1.—SUMMARY OF SPLENECTOMIES DONE ON CHILDREN UNDER 14 YEARS OF AGE—(*Continued*)

Diagnosis	Author	Age and Sex	Spleen	Blood Examination	Result	Remarks
14. Splenic anemia (Banti's)	Sutherland, G. A., and Burghard, F. F.: Treatment of Splenic Anemia by Splenectomy, Lancet **2**: 1819, 1910	12 yrs. Female	Spleen not enlarged before operation; Wt., 2 lbs.; hyperplasia of all tissues	Before splenectomy: R.B.C. 2,500,000; Hb. 40%; W.B.C. (3 mos. before) 9,800. After 3 days: R.B.C. 4,700,000; Hb. 76%. After 4 yrs.: R.B.C. 3,600,000; Hb. 78%; W.B.C. 6,400	4 yrs. after operation in good health; in service as a nurse maid	
15. Splenic anemia (Banti's)	Ibid	6 yrs. Female	Pain in splenic region 2 mos. before admission; spleen enlarged	Before splenectomy: R.B.C. 1,870,000; Hb. 30%; W.B.C. 2,400; normoblasts about 600 per cm. After 17 days: R.B.C. 5,200,000; Hb. 65%; W.B.C. 3,400	7 weeks after operation improvement continuing	
16. Banti's disease	Luce, H.: Zur Pathologie der Bantischen Krankheit, Med. Klin **6**: 535, 1910	6 yrs. Female	Spleen noted large 3 mos. before operation; Wt., 240 gm.; pulp filled with R.B.C.; lymphatic elements reduced; fibrous tissue reduced; malpighian bodies more numerous and larger	Before splenectomy: R.B.C. 1,400,000; Hb. 20%; W.B.C. 11,980. After 1 yr.: R.B.C. 4,100,000; Hb. 65%; W.B.C. 8,600; P. 45.8%; L. 45.3%; L.M. and Tl. 3%; E 7.5%	One year after operation in excellent health	
17. Splenic anemia	Giffin, H. Z.: Private communication	2½ yrs.	Chronic splenitis	Before splenectomy, 1 day: R.B.C. 2.1; Hb. 18%; W.B.C. 5,800. After 1 mo.: R.B.C. 2.32; Hb. 18%; W.B.C. 14,400	.....	Symptoms noted 1 mo. before operation. Urine exam. 1 da. previous to operation: Amt. 200; Sp. Gr. 1.004; React. alk.; Alb. 2
18. Splenic anemia	Ibid	8 yrs.	Chronic splenitis (fairly marked fibrosis); multiple small hemorrhagic areas scattered throughout spleen	Before splenectomy, 4 days: R.B.C. 4.53; Hb. 75%; W.B.C. 2,800. 28 days after: R.B.C. 4.53; Hb. 68%; W.B.C. 15,000	.....	Symptoms noted 3 mos. before operation. Urine exam. 14 da. previous to operation: Amt. 400; Sp. Gr. 1.026; React. acid; negative
19. Splenic anemia	Ibid	2½ yrs.	Chronic splenitis; marked fibrosis; multiple small hemorrhages throughout	Before splenectomy, 26 days: R.B.C. 2.57; Hb. 38%; W.B.C. 5,400. After 5 days: R.B.C. 4.41; Hb. 72%; W.B.C. 21,800	.....	First hemorrhage 18 days before operation; tumor 6 mos. Urine exam. 25 da. prev. to operation: Amt. 200; Sp. Grav. 1.023; React. acid; Alb. 1; Pus 1
20. Splenic anemia	Ibid	8 yrs.	Chronic splenitis	Before splenectomy, 5 days: R.B.C. 2.82; Hb. 35%; W.B.C. 8,200. After 26 days; R.B.C. 2.62; Hb. 32%; W.B.C. 12,000	Died 2½ months after operation	Symptoms noted 2 mos. before operation. Urine exam. 1 mo. previous to operation: Amt. 850; Sp. Gr. 1.014; React. acid; Alb. 2
1. Tuberculosis....	Ibid	10 yrs.	Chronic splenitis with localized areas of miliary tuberculosis	Before splenectomy, 23 days: R.B.C. 4.40; Hb. 35%; W.B.C. 7,900. After 13 days: R.B.C. 4.04; Hb. 40%; W.B.C. 18,000	.....	Symptoms 2 yrs. before operation. Urine exam. 23 da. previous to operation: Amt. 350; Sp. Gr. 1.019; React. acid; Alb. 0; pus negative

1. Septic splenomegaly	Ibid	10 yrs.	Reddish spleen with numerous malpighian bodies; slight increase fibrous tissue; spleen is color of splenomyelogenous leukemia	Before splenectomy, 5 days: R.B.C. 4.14; Hb. 61%; W.B.C. 6,800. After 15 days: R.B.C. 3.42; Hb. 45%; W.B.C. 14,200	Died 7 mos. after operation	Symptoms for 8 wks. 2 trans. pre-op. Urine exam. 6 da. previous to operation: Amt. 400; Sp. Gr. 1.027; React. acid; Alb. 1; pus negative
1. Hemolytic jaundice (congenital)	Nobel: Berl. Klin. Wchnschr. **51**: 1150, 1343, 1914; report taken from Elliott and Kanavel: Splenectomy and Hemolytic Ieterus, Surg., Gyn. & Obst. **21**: 32, 1915	Child Male	Enlarged spleen noted.....	Before splenectomy: R.B.C. 800,000 (half nucleated); Hb. 15%; W.B.C. 100,000. After: R.B.C. 3,600,000; Hb. 47%; W.B.C. 10,000	Rapid recovery after operation; jaundice gone	Jaundice and urobilinuria noted 1 mo. before operation; this reference not verified in original article; fragility R.B.C. increased
2. Hemolytic jaundice (congenital)	Ibid	8 yrs. Male	3 fingers below costal morgin	Before splenectomy: R.B.C. 2,600,000; Hb. 46%. After 10 days: R.B.C. increased; Hb. 71%	Jaundice gone after 10 days	Jaundiced soon after birth; yellow since then; urobilinuria; fragility of R.B.C. increased
3. Hemolytic jaundice (probably congenital)	Römer: München. med. Wchnschr. 1914, No. 9 50; also Wien. Med. Wchnschr. **64**: 1029, 1914; taken from Elliott and Kanavel's table (see No. 1)	11 yrs	.....	Blood entirely normal after operation	Jaundice disappeared; blood normal; cured; (no date given)	
4. Hemolytic jaundice (type not indicated)	Pollitzer, H.: Fall von Splenomegalia haemolytica, Wien. klin. Wchnschr. **26**: 952, 1913	13 yrs. Female	Spleen noted large at 2 yrs.; Wt., 650 gm.	Slight anemia, excess of leukocytes; polychromasia normoblasts (no counts given)	Jaundice disappeared after operation	Urobilin in both urine and stools before operation
5. Hemolytic jaundice (type not indicated)	Graf, P.: Zur Chirurg. Therapie des haemolyt. Ikterus, Deutsch. Ztschr. f. Chir. **130**: 462, 1914	13 yrs. Female	.....	Before splenectomy: R.B.C. 2,600,000; Hb. 40%; W.B.C. 11,600. After 10 mos.: R.B.C. 6,900,000; Hb. 80%; W.B.C. 11,400	10 mos. after operation patient was strong and able to work; countenance somewhat yellow; liver still large	Urine contained urobilinogen; none after operation
6. Hemolytic jaundice (type not indicated)	Schneider, J. P.: Two Splenectomized Cases Minn. Med. **2**: 210, 1919	13 yrs. Female	.....	Before splenectomy: R.B.C. 2,904,000; Hb. 49%; W.B.C. 4,500; P. 60%; L.L. 15%; S.L. 24%; E. 5%; anisocytosis marked. After 15 days: R.B.C. 3,975,000; Hb. 58%; W.B.C. 12,000	Well 6 mos. after operation	Abdominal distention noted for 2 years past; urine: urobilin and urobilinogen in large amounts before operation; none 9 days after operation
7. Hemolytic jaundice (type not indicated)	Giffin, H Z.: Hemolytic Jaundice, a Review of 17 Cases, Surg., Gyn. & Obst. **25**: 152, 1917	9 yrs. Male	Wt., 1,370 gm.	Before splenectomy: R.B.C. 1,340,000; Hb. 24%; W.B.C. 15,200; P. 59%; S.L. 29%; L.L. 4%; E. 2.3%; Baso. 2.7%; Megal. 3%; normoblasts 57 to 300 W.B.C. After 18 days: R.B.C. 2,260,000; Hb. 38%; W.B.C. 12,600; P. 64%; S.L. 16.3%; L.L. 10.7%; E. 6.7%; Baso. 1.7%	1 yr. and 3 mos. after operation in excellent health	
8. Hemolytic jaundice	Whipham, T. R. C.: Splenomegalic Hemolytic) Jaundice, Lancet **2**: 1194, 1914	6 yrs. Female	Enlarged 3 mos. before operation	Before splenectomy: R.B.C. 994,000; W.B.C. 13,180. After 3 mos. and day before death: R.B.C. 5,500,000; Hb. 70%; W.B.C. 23,400; Index 63	Died 3 mos. after operation	Jaundice at birth; lasted 6 wks.; good health until 3 mos. before operation; urine before op. contained bile pigment, also before death; day before death jaundice and epistaxis

TABLE 1.—SUMMARY OF SPLENECTOMIES DONE ON CHILDREN UNDER 14 YEARS OF AGE—(*Continued*)

Diagnosis	Author	Age and Sex	Spleen	Blood Examination	Result	Remarks
9. Hemolytic jaundice	Box, C. R.: Case of Excision of Spleen for Congenital Family Cholemia, Proc. Roy. Soc. Med. **6**: Dis. Child. Sec. 8, 1913	12 yrs. Female	Enlargement of spleen since infancy; Wt., 390 gm.; moderate perisplenitis; splenic tissue had undergone fibrosis; sinuses dilated	Before splenectomy: R.B.C. 3,337,000; Hb. 65%; W.B.C. 10,640; P. 50%; S.L. 4%; L.L. 3.75%; large hyalin cells 3.5%; E. 2.25%. After 5 wks.: R.B.C. 3,868,750; Hb. 75%; W.B.C. 21,280; P. 50.25%; S.L. 25.25%; L.L. 3.75%; E. 13.5%; large hyalin cells 6%; mast cells 1.25%	5 wks. after operation much improved; 5 days later died; uremic convulsions. P.M.: abscesses in splenic stump and nephritis	Jaundice for 6 wks. after birth
10. Hemolytic jaundice (author regards diagnosis as somewhat doubtful)	McKendrick, J. S.: Anemia with Enlargement of the Spleen, Practitioner **93**: 660, 1914	8 yrs. Male	No history of enlargement; Wt., 4.7 oz.; pulp, majority of cells lymphocytes; few normoblasts; considerable noneutrophilic and erosinophilic polymorphonuclears	Before splenectomy: R.B.C. 2,550,000; Hb. 25%; W.B.C. 7,800; differential normal; anisocytosis; poikilocytosis; polychromatophilic; few normoblasts. After 3 mos.: R.B.C. 4,890,000; Hb. 75%; W.B.C. 12,000; P. 62%; L.M. 5%; megalocytes 6%; no nucleated R.B.C.	22 months after, healthy appearance; no trace of anemia	No history of spleen enlargement; ill health and anemia for 4 years
11. Hemolytic jaundice	Arschütz: Hemolytic Jaundice Cases (see Elliott and Kanavel's table)	13 yrs. Female	No report	No report	Afterward entirely healthy	Had epileptiform attacks 2 days after operation; did not recur
12. Hemolytic jaundice	Giffin, H. Z.: Private communication	9 yrs.	Chronic splenitis	Before splenectomy, 9 days: R.B.C. 1.34; Hb. 24%; W.B.C. 15,200. After splenectomy 18 days: R.B.C. 2.16; Hb. 38%; W.B.C. 12,600	.....	Jaundice from birth; more marked at times; Splen. 1½ yrs. Hist. of jaundice in family: mother's cousin; increased fragility R.B.C. Urine ? da. pre.-op.: Amt. 750; Sp. Gr. 1.013; React. acid
13. Hemolytic jaundice	Ibid	11 yrs.	Chronic splenitis	5 days before splenectomy: R.B.C. 3.59; Hb. 56%; W.B.C. 11,000. After 6 mos.: Hb. 95+% (elsewhere)	.....	Jaundice 6 yrs.; Splen. 6 mos. Hist. jaun. in family: father hemolytic jaundice; increased fragility R.B.C. Urine 5 da. pre.-op.; Amt. 960; Sp. Gr. 1.014; React. acid; Alb. 0; neg.
14. Hemolytic jaundice	Ibid	11 yrs.	Chronic splenitis; thick, red fairly firm spleen	Before splenectomy, 11 days: R.B.C. 2.69; Hb. 52%; W.B.C. 9,600. After 21 days: R.B.C. 4.24; Hb. 58%; W.B.C. 5,200	.....	Jaundice from birth; Splen. 6 mos.; no family hist. of jaundice; increased fragility R.B.C. Urine 9 da. pre.-op.: Amt. 780; Sp. Gr. 1.021; React. acid; Alb. 2; pus 1
15. Hemolytic jaundice	Ibid	8 yrs.	.....	Before splenectomy, 14 days: R.B.C. 4.0; Hb. 68%; W.B.C. 7,200. After 9 days: R.B.C. 5.37; Hb. 78%; W.B.C. 13,600	Died 2 mos. after operation	Jaundice 1 yr. ago for 1 wk.; pain 3 mos.; no family hist. of jaundice; increased fragility R. B. C. Urine 14 da. pre.-op.: Amt. 500; Sp. Gr. 1.012; React. acid; Alb. 0; negative

1. Gaucher's disease	Herman, C., and others: Case of Gaucher's Disease in a Boy 13 Years of Age, Arch. Pediat. **31**: 340, 1914	13 yrs. Male	Wt., 1,320 gm.; 27×13×10 cm.; many large endothelial cells with irregular outline; one or more nuclei; round of ovoid venous sinus greatly distended	Before splenectomy: R.B.C. 3,900,000; Hb. 45%; W.B.C. 4,000; P. 48%; L. 50%; E. 2%. After 2 mos.: R.B.C. 3,300,000; Hb. 52%; W.B.C. 15,000; P. 62%; L. 35%; E. 3%	Improved greatly after operation	Enlargement of abdomen at 4 yrs.; at 7 yrs. spleen 8 cm. below umbilicus and 1 cm. beyond navel in median line
2. Gaucher's disease	Erdmann, J. F., and Moorhead, J. J.: Splenectomy for Splenomegaly (Gaucher type), Am. J. M. Sc. **147**: 213, 1914	3½ yrs. Female	Spleen enlarged 2 yrs. before, slightly; great numbers of large mononuclear cells throughout, occasionally more than one nucleus in a cell; malpighian bodies few	Before splenectomy: R.B.C. 6,200,000; Hb. 85%; W.B.C. 7,000; normal differential. After 10½ mos.: R.B.C. 5,300,000; Hb. 75%; W.B.C. 16,000; normal differential	16 mos. after operation child is reported well and strong	
3. Gaucher's disease	Mandlebaum, F. S.: Contribution to the Pathology of Primary Splenomegaly (Gaucher type), J. Exper. M. **16**: 797, 1912	4½ yrs. Male	Spleen found large 1 yr. before operation; alveolar spaces with large cells identical to those of Gaucher's disease; malpighian bodies unusually large size	Before splenectomy: R.B.C. 4,000,000; Hb. 68%; W.B.C. 4,200; P. 70%; L.L. 25%; Mono. 1%; Myelo. 1%; slight poikilocytosis and anisocytosis. After: R.B.C. 3,800,000; Hb. 66%; W.B.C. 19,600; normal differential	Child died day following operation	
4. Gaucher's disease	Foot, N. C., and Ladd, W. E.: Report on a Case of Gaucher's Splenomegaly, Am. J. Dis. Child. **21**: 426 (April) 1921	8 yrs. Male	Spleen 1 cm. below costal margin about 7 yrs. of age; Wt., 305 gm.; 14×6×5; large cells typical of Gaucher's disease, filled the venous sinuses and pulp spaces so completely as to transform the picture into one resembling alveolar tumor	Before splenectomy: R.B.C. 5,808,000; Hb. 90%; W.B.C. 6,600; P. 49%; L.L. 19%; S.L. 30%; Mononu. 3%; 1 myelocyte noted. After: R.B.C. 4,976,000; W.B.C. 18,800; P. 48%; L. 41%; E. 1%; Monos. 10%; R.B.C. normal	4 mos. after operation gained 2 lbs. general health improved; attending school regularly	Fullness in flank noticed about 4 yrs. of age. Symptoms: pain in abdomen and legs and profuse sweating
Unclassified Cases:						
1. Large cell splenomegaly	Jonz, R. de Josselende and von Heukelom, T. S.: Beitrag zur Kenntnis der grosszelligen Splenomegalie, Beitr. z. path. Anat. **48**: 598, 1910	12½ yrs. Female	Malpighian bodies and pulp consist of alveolar connective tissue filled with large, irregular shaped cells with one or more nuclei	Before splenectomy: R.B.C. 4,782,000; Hb. 65%; W.B.C. 3,800. After 6 mos.: R.B.C. 4,920,000; Hb. 80.85%; W.B.C. 14,400; P. 54%; S.L. 18.6%; L.L. 10.6%; L.Mono. and T. 6.8%; E. 10%	6 mos. after operation general condition fairly good, but slight jaundice and enlargement of liver	At 7½ yrs. of age abdomen had begun to enlarge; liver and spleen both large
2. Possible hemolytic jaundice	Sutton, J. Bland: Three Successful Splenectomies, Lancet **2**: 974, 1895	5 yrs. Female	Wt., 10 oz.; no pathologic report	None	Recovered and seemed in excellent health	Author belives it to be a case of hemolytic jaundice such as he had seen in an older patient before; no symptoms reported
3. Possible Banti's disease	Thursfield, H., and Gow, A. E.: Splenomegaly; Splenectomy, St. Barth. Hosp. Rep. **50**: 7, 1914	10 yrs. Female	No report	Before splenectomy, 18 mos.: R.B.C. 4,630,000; Hb. 72%; W.B.C. 12,000	Died 48 hours after operation	Called "splenomegalic cirrhosis of liver"
4. Enlarged spleen with anemia	Barling, G.: Splenectomy for Enlarged Spleens with Anemia, Lancet **1**: 220, 1915	6 yrs. Female	No report	Before splenectomy: R.B.C. 3,300,000; Hb. 70%; W.B.C. 26,000. After: no count	Died 4th day after operation	Condition of liver after operation suggested delayed anesthetic poisoning
5. Splenomegaly...	Nixon, J. A.: Splenectomy for Splenomegaly, Bristol M. Clin. J. **31**: 325, 1913	14 yrs. Female	No history of enlargement until time of first examination; 7×3 in.; enlargement due to simple hyperplasia of normal spleen tissue	Before splenectomy: R.B.C. 5,000,000; Hb. 50%; W.B.C. 17,000; P. 55%; L.Mono. 14%; S.Mono. 26%; E. 5%; no abnormal cells. After 4 mos.: R.B.C. 4,200,000; Hb. 80%; W.B.C. 9,200; P. 52%; S.Mono. 37%; L. Mono. 7%; E. 3%	For a year after operation, remained well; later developed symptoms of pulmonary tuberculosis	Strong and well until 1 year before operation

disease, 4; hemolytic jaundice, 15; tuberculosis, 1; septic splenomegaly, 1; unclassified cases, 5. Splenic anemia and Banti's disease have been classified together because it is generally accepted that the designation "splenic anemia" in most instances probably corresponds to the early stages of Banti's disease.

A study of the case reports would justify the statement that splenectomy had been resorted to in most instances to save life. One wonders if removal of the spleen may not be considered as a measure to conserve life. If this be so a decision to remove it in the early stages of the pathologic processes is important.

Table 2 summarizes the incidence of spleens which extend 2 cm. or more below the costal margin. The measure, 2 cm., is chosen arbi-

TABLE 2.—SHOWING DISEASES AND NUMBER OF CASES OUT OF 2,000 WITH SPLEEN 2 CM. OR MORE BELOW THE COSTAL MARGIN (BABIES' HOSPITAL, NEW YORK CITY)

Diagnosis	No. of Cases	Measurement of Spleen Below Cm.		Average Age, Months	Sex	
		Average	Maximum		Male	Female
1. Tuberculosis, general miliary	17	2¾	6	12¼	10	7
2. Congenital syphilis	10	4⅗	9	5 1/10	1	9
3. Bronchopneumonia	18	2½	5	12¾	10	8
4. Von Jaksch's anemia	4	7	9	6	4	
5. Rickets and complications: secondary anemia; bronchopneumonia; asthma; lobar pneumonia	9	2½	5	16	5	4
6. Chronic constipation	1	3	3	19	1	
7. Anemia, secondary and complications: follicular tonsillitis, purpura	5	5¼	7	13 1/10	3	2
8. Sarcomatosis	1	2	2	28	..	1
9. Bronchitis	2	2	2	4½	2	
10. Congenital heart disease	3	2	2	7	3	
11. Tonsillitis	1	2	2	4 yrs.	..	1
12. Marasmus and complications: gastro-enteritis; acute bronchitis; secondary anemia; bronchopneumonia	4	2	2	4	3	1
13. Nutritional edema with anemia	1	2	2	2½	1	
14. Empyema	4	2½	3	10⅘	3	1
15. Fistula: vesico and rectovaginal	1	3	3	11	..	1
Total number of cases	81	...	...	..	46	35

trarily as representing a large spleen. Fifteen diseases are recorded in this tabulation. With the exception of von Jaksch's anemia (possibly, also some of the cases classified under anemia) the other fourteen diseases must be differentiated from those conditions to which splenectomy is applicable. No instance of leukemia appears in this chart. This disease, perhaps above all others, must be excluded in a decision to remove the spleen. Removal of the spleen in leukemia is contraindicated.

Three cases are presented herewith as a contribution to the literature of splenectomy. From an analysis of their history, symptoms and physical signs, an attempt will be made to derive certain criteria, which may aid to indicate under what circumstances splenectomy is justifiable.

REPORT OF CASES

CASE 1.—This case is of special interest as the boy has been since 3 months of age under the care of Dr. F. Elmer Johnson of New York, who referred him to the Babies' Hospital.

History.—T. M. was admitted March 5, 1920, at 5 years of age, for a blood transfusion. Five days before he was admitted it was noticed that he was pale; and two days before his admission he vomited blood, and blood was noticed in his stool.

Family History.—Father and mother are in good health. Two other children are living and well. There is no history of jaundice in the family.

Birth History.—He was full term; the labor was normal, and the birth weight is reported as being 10 pounds.

Feeding History.—He was breast fed for six months after which he received milk and barley water mixtures. At one year he was given solid food. His nutrition was always excellent.

Previous Illnesses.—He was always healthy up to the age of 3½ years when he first vomited blood. The mother stated it was about a cupful. Afterward he became pale and listless and stayed so for six months. He then began to improve and his color returned. When he was 4½ years old he vomited blood again. This time the quantity was said to be larger. He was pale and listless for about three months when he began to pick up and his color returned. At 4 years of age he went to St. Luke's Hospital, New York, because of an attack of diarrhea. He received at the same time radium treatment for an enlarged spleen. He returned to St. Luke's Hospital three times between the ages of 4 and 5 for radium treatment.

After his third treatment, April 30, 1920, he became pale. Three days later he vomited blood and passed black stools. Because of weakness and inability to be up and about he was sent to the Babies' Hospital for transfusion.

The enlargement of the spleen was first noticed at 3 months of age. It measured two inches from the costal margin. Dr. Johnson observed particularly that the spleen was "prominent on the abdominal wall."

Summary of History.—Vomiting of blood occurred, therefore, three times between birth and 5 years of age: first at 3½ years; a second time at 4½ years; and a third time at 5 years. Enlargement of the spleen was first noted when he was 3 months old. Four radium treatments for an enlarged spleen had been given at St. Luke's Hospital within the year before his admission to the Babies' Hospital. They apparently were of no avail in diminishing the size of the spleen nor in checking hemorrhage.

Physical Examination.—General appearance was that of a well developed and well nourished white boy. He was rather pale. Mucous membranes were pale. Heart: Normal in size; the sounds were of good quality; a soft blowing systolic murmur was heard at the apex and along the left border of the sternum. Liver: Not felt. Spleen: Measured 7 cm. from the costal margin to the tip and 7.6 cm. from side to side. In all other respects the physical examination was normal.

Blood Examination, Before Transfusion.—Red blood cells, 3,200,000; hemoglobin, 30 per cent.; white blood cells, 6,000; polymorphonuclears, 70 per cent.; lymphocytes, 30 per cent.

He was transfused May 5, 1920, with 230 c.c. of blood from a cousin.

Blood Examination May 6, 1920 (day after transfusion).—Red blood cells, 4,160,000; hemoglobin, 55 per cent.; polymorphonuclears, 80 per cent.; lymphocytes, 20 per cent.

Marked achromia and slight variation in size of the red cells. No normoblasts nor megaloblasts seen. Pirquet test negative.

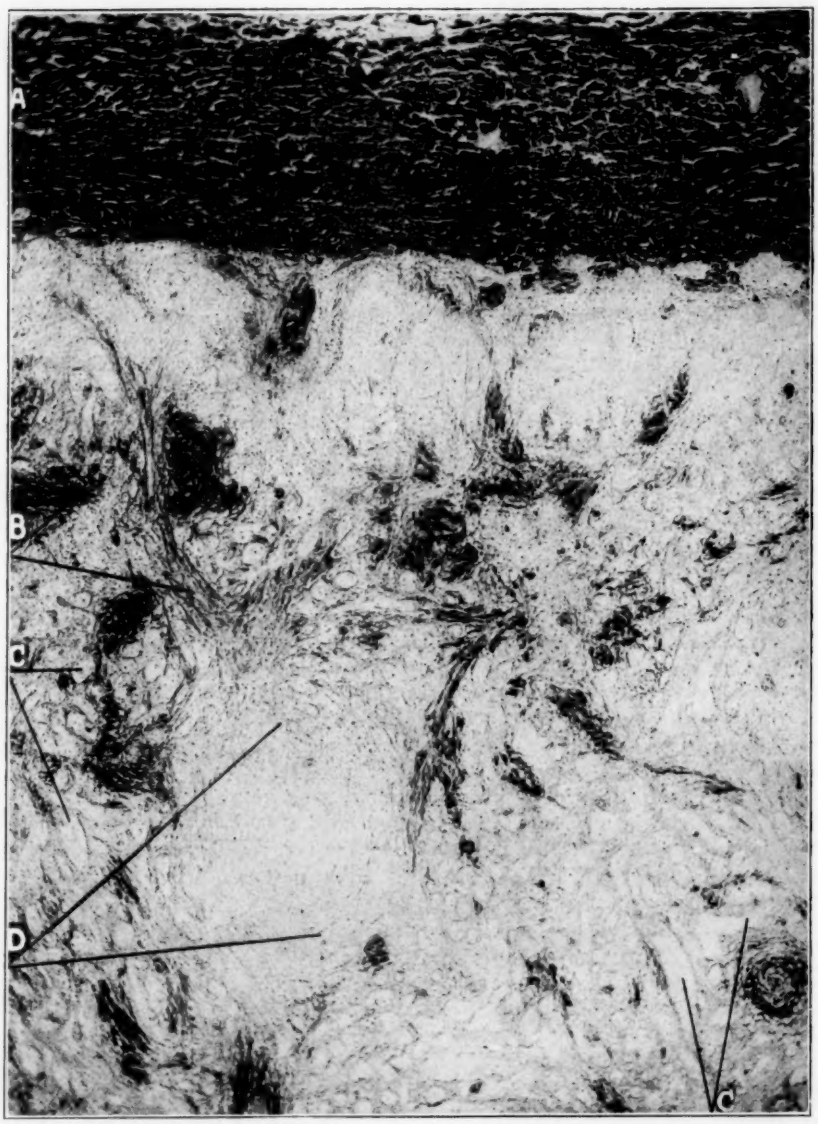

Fig. 1.—Section of spleen of Banti's Disease, Mallory's connective tissue stain. *a*, capsule; *b*, trabeculae; *c*, dilated venous spaces; *d*, malpighian body; ×135.

The temperature on admission was 99; the day following transfusion it rose to 101.4 F; and on the day of his discharge it was 99.6 F.

He was discharged May 7 against advice, with the diagnosis of chronic secondary anemia.

Second Admission.—Nov. 3, 1920, T. M. was readmitted to the hospital. The occasion for his return was "bleeding from the rectum." The statement was made that two days before admission he passed about "half a chamberful of blood." It was estimated that there was about one quart of clotted blood and feces. On the day of admission there was another "bleeding from the rectum."

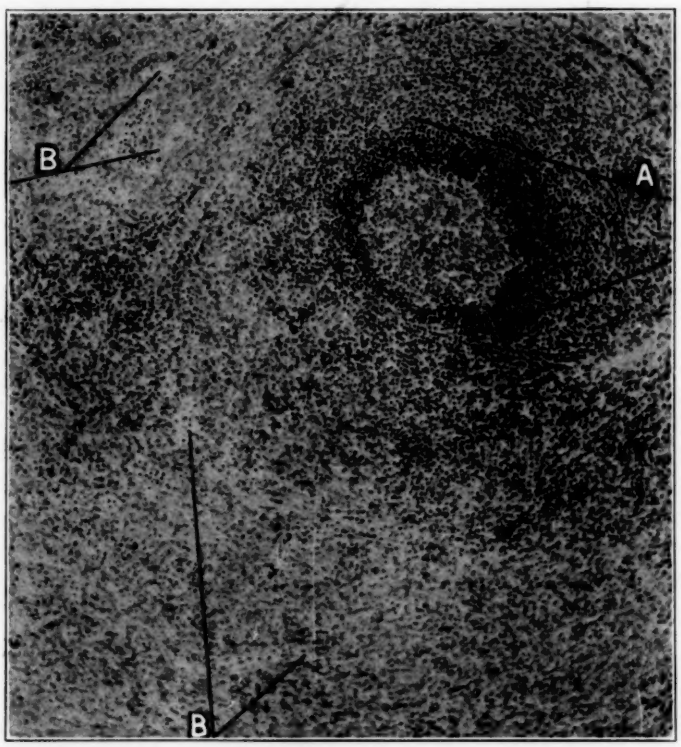

Fig. 2.—Section of spleen of Banti's Disease; *a*, malpighian body with Keim center; *b*, dilated venous spaces; × 135.

On his first admission in May no special information was obtained about the loss of blood by way of the rectum. The history obtained at that time was of repeated vomiting of blood. It mentioned casually that tarry stools had been observed.

The first hemorrhage by way of the lower bowel occurred at 2½ years of age. From that time to Nov. 20, 1920, he had about five similar attacks separated by several months' intervals. The losses of blood were, as a rule, repeated over a period of one or two days. He became pale at the time of the attack but would regain color until the next hemorrhage.

The diagnosis on readmission was duodenal ulcer.

The physical examination added only the following information: enlargement of the tonsils and carious teeth. The spleen measured 9 cm. from the costal

margin to its tip; six months before it measured 4 cm. The weight was 49½ pounds. The blood count was as follows: Dec. 1, 1920: Red blood cells, 3,702,000; hemoglobin, 45 per cent.; leukocytes, 4,400; polymorphonuclears, 71 per cent.; lymphocytes, 29 per cent.; small lymphocytes, 22 per cent.; large lymphocytes, 7 per cent. The red cells showed slight acromia. One normoblast was seen in counting 100 white cells. Stool was negative for blood.

December 8: Removal of the spleen was decided on. The reason for this decision was in the nature of a counsel of desperation. The transfusion in May had proved unavailing in preventing a recurrence of the hemorrhages and in determining any improvement in the blood condition.

December 10: Transfusion of 150 c.c. of blood from an uncle.

December 11: Splenectomy by Dr. William Downes. The spleen weighed 375 gm. The liver showed some thickening of the capsule and some enlargement. It was apparently not harder than normal. No ulcers were found in the pylorus or duodenum. The abdomen contained a large amount of fluid which gushed from the wound.

TABLE 3.—Record of Blood Examinations in Case 1

Date	Erythrocytes	Hemoglobin, per Cent.	Leukocytes	Polymorphonuclears, per Cent.	Lymphocytes, per Cent.	Transitionals, per Cent.	Remarks
12/ 1/20	3,792,000	45	4,400	70	29	1	Red cells show slight achromia; one normoblast to 100 leukocytes
12/ 9/20	2,160,000	35	7,800	70	30		
12/10/20	.....	..	Transfusion				
12/11/20	3,104,000	50	10,000	72	28		
12/11/20	.....	..	Splenectomy				
12/14/20	3,100,000	50	34,000	76	18	3	Large mononuclears 3%
12/17/20	3,824,000	50	13,200	72	28		
12/20/20	4,192,000	60	10,200	49	36	8	Large mononuclears 7%
12/23/20	5,168,000	65	17,000	68	32		
12/26/20	4,176,000	70	10,200	64	25	6	Large mononuclears 5%
12/30/20	4,224,000	70	10,000	55	45		
1/ 3/21	4,400,000	65	9,800	56	44	..	Discharged on this date
5/16/21	5,192,000	70	10,200	74	26	..	Returned for blood examination 6 mos. after splenectomy. Test for fragility of R. B. C. normal

Jan. 3, 1921: The patient was discharged from the hospital. The convalescence from the operation was most satisfactory. The day following the splenectomy the temperature rose to 104.4 F.; the second day to 102 F.; the third day to 101.4 F.; the fourth day to 101.2 F. From this time on to his discharge the temperature was normal.

Urine Examination.—Repeated examinations showed a normal urine. No tests for urobilin were made. Pirquet test was negative. Wassermann was negative.

The condition of the child May 16, 1921, five months after operation has been kindly furnished by Dr. F. Elmer Johnson in the following personal communication:

The child came to me first on June 7, 1917, at 3 months of age. The first examination revealed a spleen two inches below the costal margin. It was very hard. The baby weighed 11 10/16 pounds. A Wassermann test June 18, 1915, was negative. July 13, 1915, at four months of age, the leukocyte count was as follows: Total leukocytes, 15,000; polymorphonuclears, 15 per cent.; lymphocytes, 84 per cent.; eosinophils, 1 per cent.

May 13, 1915, the spleen was smaller. It was a question whether the mass felt was a kidney or a spleen. Oct. 25, 1915, he weighed 19 pounds. Sept. 26, 1915, he weighed 26 pounds; the hemoglobin was 30 per cent.

May 16, 1921, six months after splenectomy, the patient reported to me. He was in excellent condition. His color was that of a normal child. The mother says he behaves like a normal child except for an abnormal appetite, and restlessness at night.

PATHOLOGIC REPORT (contributed by Dr. Martha Wohlstein): *Macroscopic Examination.*—The spleen weighs 375 gm. and measures 14x8x4 cm. Its capsule is greatly thickened, grey in color, and covered with dense fibrous adhesions most numerous at the upper pole. The uncut spleen felt soft.

On section the capsule is found to measure 1 mm. in thickness. The cut surface of the splenic substance is dull red in color, smooth, rather soft and almost pits on pressure. Connective tissue septums are numerous, grey, not wide. The blood vessels are large. No areas of hemorrhage are apparent,

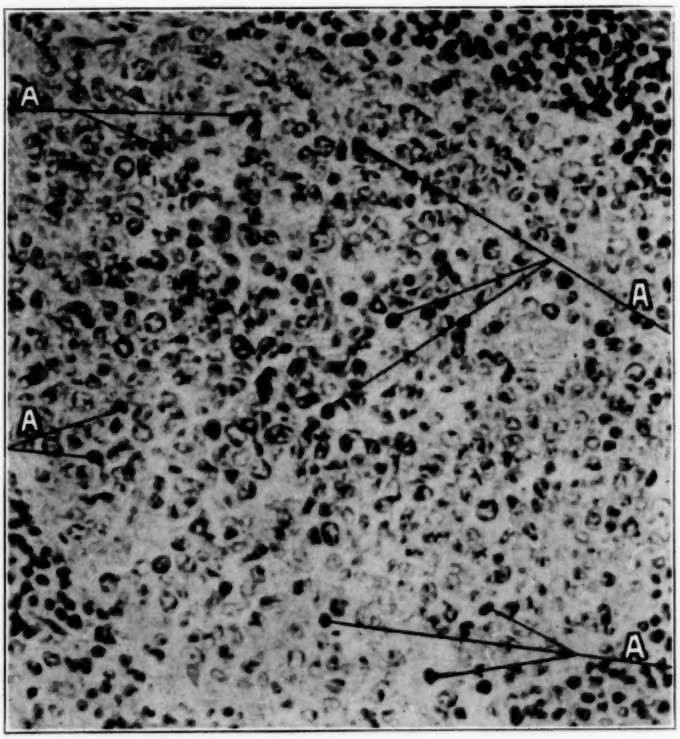

Fig. 3.—Section of spleen of Banti's Disease; Keim center of malpighian body showing kariokynetic figures in nuclei of leukoblasts, *a;* × 450.

but some congested vessels have been cut across. The malpighian bodies show as pearly grey nodules 1 mm. in diameter, and not diminished in number.

Microscopic Examination.—(Figs. 1, 2 and 3).—The capsule is fully three times thicker than normal, and composed of dense fibrous connective tissue. Blood vessels are numerous near the free surface, and small hemorrhages have occurred where these vessels were torn on removal of the organ. From the thick capsule wide trabeculae of connective tissue ramify into the spleen substance. This seems to be made up chiefly of connective tissue and venous spaces, the pulp cells being almost entirely absent from large areas. The venous spaces are dilated in many places, but not beyond a moderate degree. They contain red blood cells, mononuclear and polynuclear leukocytes, and are

lined with endothelial cells. In some places these lining cells are swollen, but they are not found free in the lumen of the blood sinuses. No mononuclear cells resembling those typical of Gaucher's splenomegaly are present, nor are the venous spaces dilated to form the alveolar arrangement typical of that lesion. With Mallory's connective tissue stain the increased amount of fibrous tissue is well shown, and the ramifications of the fibrils about the bodies are large and not less numerous than normal. Each contains a distinct germ center in which from 1 to 3 karyokinetic figures in the nuclei of leukoblasts are present. The periphery of the malpighian bodies is densely packed with mononuclear cells. Some columns of typical pulp cells are seen close to malpighian bodies.

The characteristic things about the sections are three: the marked increase in fibrous connective tissue in the capsule and in the spleen substance; the congested venous spaces; the comparatively small number of pulp cells.

The picture closely resembles that of Banti's disease.

Before presenting the second case of this series, a brief report of a case of von Jaksch's anemia with microphotographs of the spleen is introduced for comparison with Case 1. The diagnosis of von Jaksch's disease was made on the blood picture which was regarded as characteristic of that disease, and on enlargement of the spleen. The latter organ was described as follows: At the level of the umbilicus it reaches to within 1 cm. of the midline. The lower border extends 1 cm. below the level of the crest of the ileum. The blood picture was:

Oct. 10, 1917: Red blood cells, 1,472,000; hemoglobin, 9 per cent.; white blood cells, 83,000; polymorphonuclears, 23 per cent.; lymphocytes, 2 per cent.; small lymphocytes, 75 per cent. Numerous normoblasts showing mitosis, poikylocytosis, anisoscytosis, myelocytes.

Oct. 11, 1917, the child was transfused with 60 c.c. of its father's blood into the sinus. The blood picture on the next day showed:

Red blood cells, 1,784,000; hemoglobin, 15 per cent.; polymorphonuclears, 48 per cent.; large lymphocytes, 2 per cent.; small lymphocytes, 45 per cent.; myelocytes, 3 per cent.; eosinophils, 2 per cent. Normoblasts showing mitosis; megaloblasts; poikylocytosis and anisocytosis.

The infant died the following day.

Dr. Martha Wohlstein has furnished the following report on the pathologic examination of the spleen:

Microscopic Examination.—The capsule is of normal thickness; the connective tissue trabeculae are not wider than normal, and they are loosely meshed. The pulp spaces are prominent, some are empty, some contain red and white blood cells. None are closely packed, but in all nucleated red cells are numerous. The endothelial cells lining the veous spaces are distinct and normal. The pulp cells are not increased in number. The malpighian bodies are present in normal numbers, but they are less dense and smaller than usual. No germ centers are apparent in them.

The following points are characteristic of these sections: Small loosely put together or "rarified" malpighian bodies, congested venous spaces, containing numerous nucleated red blood cells; pulp cells less numerous than normal.

Dr. Wohlstein has also placed in parallel columns a comparison of the microscopic pathology of the spleen of Case 1 (Figs. 1, 2 and 3) and of the spleen of the case of so-called von Jaksch's anemia (Figs. 4 and 5).

BANTI'S DISEASE (Figs. 1, 2 and 3)	VON JAKSCH'S ANEMIA (Figs. 4 and 5)
No leukocytosis; blood picture of secondary anemia.	Leukocytosis moderate or very high. Nucleated red cells numerous.
Spleen moderately enlarged.	Spleen moderately or greatly enlarged.
Surface of spleen irregular; capsule thickened.	Surface of spleen smooth, capsule not thickened.
Connective tissue trabeculae much increased; fibrous mesh work dense.	Connective tissue trabeculae increased; fibrous meshwork loose.
Venous spaces dilated; endothelium normal; contents red and white blood cells.	Venous spaces dilated; endothelium normal; contents: leukocytes and many red blood cells.
Splenic pulp cells less numerous than normal.	Splenic pulp cells less numerous than normal.
Malpighian bodies small, less numerous than normal; "Keim" centers with normal leukoblasts.	Malpighian bodies small and rarefied; no "Keim" centers apparent.
Ascites and hepatic cirrhosis in late stage.	No ascites. Liver moderately enlarged; no cirrhosis.

These two pictures may well be two stages of the same pathologic process.

Attention is called to the microscopic examination of the spleen in Case 2 (page 300). Dr. Stout, who reported the examination, states:

> This is characteristic of Banti's disease. If, however, the child shows a blood picture of von Jaksch's anemia, the splenic picture would fit but atypically. A positive diagnosis cannot be made without the blood report.

The anomalous situation in the same child is presented of a spleen which records the changes belonging to Banti's disease, and a blood picture characteristic of von Jaksch's disease. If the two cases are a distinct entity, the logic of this situation forces one to accept this proposition: the causative agent of von Jaksch's disease has elaborated its effects in the hemopoietic system; the causative agent of Banti's disease has elaborated its effect in the spleen. The following statement of Krumbhaar is of interest in this connection:

> The anemia infantum pseudoleukaemica of von Jaksch is in all probability not an independent condition, but represents an atypical response of the infantile hemopoietic system to one or the other of the primary diseases of the blood.

It has seemed best to interrupt the plan of the paper by this discussion of von Jaksch's disease. It has been stated that von Jaksch's disease is sub judice. This discussion is for the purpose of explaining that declaration.

CASE 2.—T. R. was a patient at St. Mary's Free Hospital for Children, New York City. Dr. Charles Farr has kindly furnished the hospital records for inclusion in this paper.

History.—T. R., a female child, was admitted to St. Mary's hospital Oct. 19, 1917, at 9 years of age. The chief complaint for which she came was swelling of the abdomen. The enlargement was first noticed when the child was about 3½ years of age.

Family History.—The father and mother and seven brothers are alive and well.

Previous History.—The patient had been perfectly well until she was between 3 and 4 years of age when it was noticed that her abdomen began

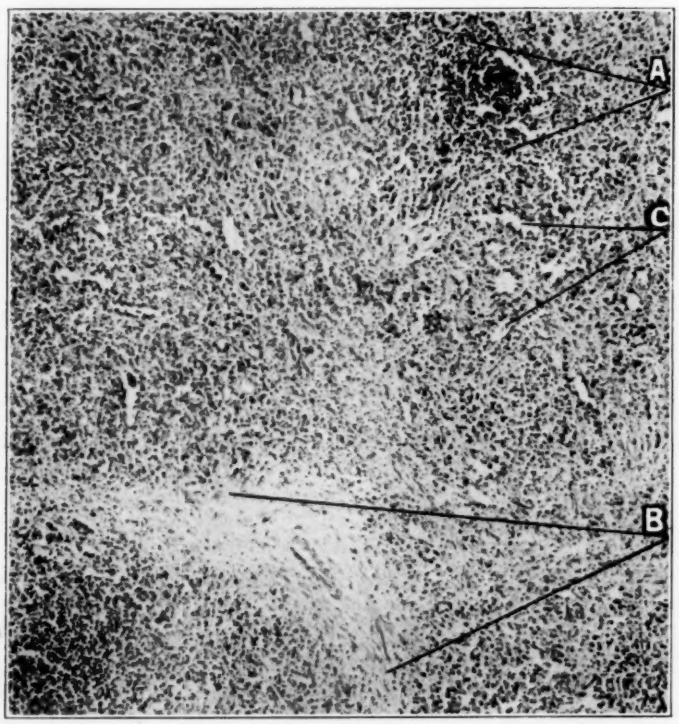

Fig. 4.—Section of spleen from case of von Jaksch's anemia. *a*, Malpighian body; *b*, connective tissue trabeculae; *c*, dilated venous spaces; × 135.

to swell. She came to the hospital June 13, and again July 16, 1917, and on each occasion her abdomen was tapped. The fluid reaccumulated. As there was no dyspnea nothing further was done until the child returned to the hospital Aug. 10, 1917, when an exploratory laparotomy was done. The belly wall was thin; the liver was small; there was no sign of cirrhosis. The spleen was enlarged and bound down everywhere by adhesions. A large mass lay over the pancreas, the relations of which were not determined. The abdomen held a large amount of fluid which was opalescent in color and clotted on standing.

The child was discharged and returned to the hospital for a third time, Oct. 19, 1917. The diagnosis at this admission was tuberculous peritonitis.

Physical Examination.—In general appearance she was much emaciated and looked chronically ill; face was pale and there were deep furrows under the eyes. Mucous membranes were pale. Teeth, carious, some missing. Tongue was furred and breath was offensive. Thorax was small and there were distended veins over the chest wall. Heart and lungs showed no abnormal signs. Abdomen: Much distended; greater in size than that of a pregnant woman (relatively). The veins in the abdomen wall were much distended. The child had to bend backward to maintain equilibrium. Fluid wave was present. Diagnosis based on physical examination was tuberculous peritonitis.

Treatment.—Oct. 19, 1917: A splenectomy was done by Dr. Charles Farr. The spleen was tremendously hypertrophied. The lower third lay behind the splenic flexure of the colon. The spleen was adherent at the upper pole to the

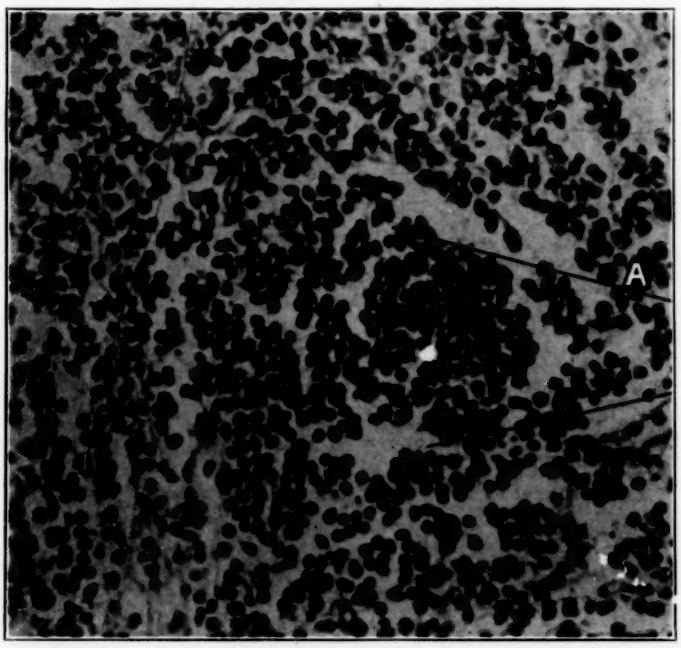

Fig. 5.—Section of spleen from case of von Jaksch's anemia. *a*. Malpighian body; *b*, dilated venous spaces containing many nucleated red blood cells; × 425.

stomach and diaphragm. On delivery the pedicle was torn and severe hemorrhage followed. The vessels were clamped and ligated. Recovery was uninterrupted.

Dec. 12, 1917: Discharged improved.

Diagnosis.—Primary splenomegaly (Banti's).

Urine Examination.—Repeated tests were negative. No mention was made of tests for urobilin.

Pirquet test was negative.

REPORT OF PATHOLOGIC EXAMINATION OF THE SPLEEN

Gross Examination.—The spleen measures 20x7x5 cm. The consistency was soft; the capsule was thickened. Recently found adhesions covered the organ. Cross section showed a pultaceous, red pulp with moderately thickened septums

and somewhat indistinct follicles. Increase in size of the spleen was due to hyperplasia of the pulp and of connective tissues.

Microscopic Examination.—Connective tissue was markedly increased throughout the pulp. The follicles were very small and far apart. The trabeculae were much thickened; the capsule was thickened and showed hyaline degeneration.

The pulp showed large and small lymphocytes and some swollen endothelial cells lining the capillaries. No myelocytes were found. This is characteristic of Banti's disease. If, however, the child shows a blood picture of von Jaksch's anemia the splenic picture would fit but atypically. A positive diagnosis cannot be made without the blood report (Dr. Stout).

TABLE 4.—RESULT OF BLOOD EXAMINATIONS IN CASE 2

Date	Erythrocytes	Hemoglobin, per Cent.	Leukocytes	Polymorphonuclears, per Cent.	Lymphocytes, per Cent.	Transitionals, per Cent.	Large Mononuclears, per Cent.	Basophils, per Cent.	Eosinophils, per Cent.	Remarks
8/ 3/17	4,340,000	68	3,600	72	19	..	4	2	3	R.B.C. pallor marked. Poikilocytosis
9/ 7/17	3,440,000	65	5,800	62.7	18.2	1.8	12.7	1	3.6	R.B.C. pallor marked. Polychromatophilia. Poikilocytosis
10/ 4/17	3,968,000	..	4,100	65	31	1	..	2	1	
10/17/17	3,200,000	65	6,000	67	28	2	3			
10/19/19	.....	..	Splenectomy							
10/28/17	2,700,000	56	25,000	80	17	2	1			
11/ 2/17	.....	..	25,000	73	19	3	5			
11/ 4/17	3,000,000	56								
5/18/21	6,240,000	70	9,800	45	40	6	5	..	4	This count is about 3½ years after splenectomy

ANALYSIS OF CASES 1 AND 2 WITH REFERENCE TO CRITERIA FOR SPLENECTOMY

The pathologic examination of the spleens of both these cases shows the changes which belong to Banti's disease. They will, therefore, be discussed together. An attempt will be made to select the salient points which collectively serve as a guide in a decision to remove the spleen.

Age of Onset.—It is impossible to state with definiteness in either case the time when the disease began. If an enlarged spleen is evidence that an abnormal condition exists the statement may be hazarded that the first stage of Banti's disease was present in Case 1 at 3 months of age.

Textbooks place the onset of Banti's disease late in childhood. "The onset is late in childhood, usually not before the tenth year, and the progress is slow (Holt)."

It seems reasonable to assume that the enlargement of the spleen in Case 1, noticed at 3 months of age, was determined by the abnormal processes which later, at the age of 3 or 4 years, manifested themselves

in the symptoms and physical signs which the pathologic examination of the spleen proved to be those of Banti's disease. It would seem absurd to assume that the enlargement of the spleen at three months was in response to an abnormal stimulus which is distinct from that which causes Banti's disease in view of the fact that the same spleen which was removed when the child was 5½ years of age, showed the changes belonging to Banti's disease. It seems probable that this spleen at 3½ months of age was the precursor of the later spleen.

T. R. (Case 2), had an exploratory laparotomy done when she was 9 years of age. The spleen was found to be enlarged. There is no history that the spleen was felt before that date. The abdomen began to swell when the child was between 3 and 4 years of age. The child was tapped at that time and fluid withdrawn. The ascites which was present was doubtless related to the same causes which produced the enlarged spleen. The onset in Case 2 was probably as early as 3½ years of age.

Therefore, Case 1 presents a probable onset at 3 months of age, and Case 2 at about 3½ years of age.

Attention is called to the possibility of an early onset of Banti's disease. If a splenectomy for this condition offers hope of a cure, the operation should be done before the advanced changes have taken place in the liver. May one be sure that an early splenectomy will forestall the cirrhotic changes in the liver? This assurance cannot be made. It may, however, be stated that a splenectomy, even after the disease has progressed to the late stage, results in an improvement in both symptoms and physical signs in a certain number of individuals, and that a splenectomy done in the early stages of the disease may, at least, delay the progress of the disease with its associated symptoms of hemorrhage, ascites, anemia, etc.

It is not known what part the spleen plays as a causative factor in Banti's disease.

The unquestioned improvement that usually follows splenectomy indicated that the altered spleen is in some way an important pathogenic factor. This is still further emphasized by Umber's unique observation. A boy, 15 years of age, was splenectomized for Banti's disease, and during the operation a small piece of the enlarged liver was excised for histological examination and a distinct peripheral infiltration of the lobules found. Later the liver reduced to normal size, a strong indication of the splenogeneous origin of the hepatitis, which, if undisturbed, should have progressed to the usual cirrhosis (Krumbhaar[1]).

Enlargement of the Spleen.—The tip of T. M.'s spleen (Case 1) was felt 5 cm. below the costal margin when he was 3 months of

1. Pearce, M. P.; Krumbhaar, E. B., and Frazier, C. H.: The Spleen and Anemia, Experimental and Clinical Studies, Philadelphia, J. B. Lippincott & Co., 1918, p. 251.

age. T. R.'s spleen (Case 2) was found to be enlarged when her abdomen was explored at about 8½ years of age.

The histologic examination of both spleens showed the changes belonging to Banti's disease (Figs. 1, 2 and 3 for T. M.'s spleen).

The diseases with which enlarged spleens are associated are analyzed in Table 2. From an examination of this table it will be seen that enlarged spleen is associated with a large number of abnormal conditions.

It is impossible to define the phrase "an enlarged spleen." If the edge of the spleen is felt just below the costal margin, the spleen is larger than normal. If the edge of the spleen is felt 2 cm. or more below the costal margin, it certainly is a warning to determine the pathologic condition with which such an enlargement is associated. The importance of such determination is obvious since indications for the removal of the spleen are limited. It becomes necessary, therefore, to exclude a large number of diseases with which splenomegaly is associated before considering splenectomy.

Emphasis is made: *First, that a distinctly enlarged spleen may be part of a pathologic condition the relief or cure of which depends on the removal of the spleen; and second, that such an enlargement may be present in the first year of life.*

Blood Examination: *Anemia.*—A study of blood examinations of Cases 1 and 2, shows in each instance a diminution of the number of erythrocytes, a hemoglobin percentage below normal, and a leukopenia. The erythrocytes showed poikilocytosis, polychromatophilia, and marked pallor.

These blood findings define a secondary anemia. This type of anemia is characteristic of Banti's disease.

Evidence of blood destruction furnished by the erythrocytes (poikilocytosis, etc.) is regarded as an indication that the disease is progressive. Therefore, blood destruction without active blood regeneration (normoblasts, reticulated erythrocytes, Howell-Jolly bodies, etc.) following transfusion furnishes a point in favor of splenectomy in the pathologic condition represented in these cases.

A leukopenia is usually associated with secondary anemia in Banti's disease; it was present in both cases.

When T. M. (Case 1) was 18 months old, Dr. Johnson found the hemoglobin to be 30 per cent. This observation is significant. At 18 months of age, therefore, there was a combination of splenomegaly and anemia. No erythrocyte count was made at this time.

A leukocyte count was made when the child was 6 months of age showing the total to be 15,000 cells of which the lymphocytes were 84 per cent. The increase of leukocytes at this period in association with an enlarged spleen might suggest von Jaksch's disease. This is

further emphasized by the predominance of lymphocytes. On the other hand, the fact that T. R.'s spleen showed characteristics of Banti's disease might throw doubt on the existence of von Jaksch's disease as a distinct entity. A comparison of the histology of Banti's disease and von Jaksch's disease is furnished in the accompanying illustrations.

It is not intended to postulate that von Jaksch's and Banti's disease are identical by the citation of the leukocyte count of T. R.'s blood when he was 6 months old. Attention is called to it in the hope that further information may be forthcoming.

The effects of transfusion on T. R.'s anemia is shown in Table 4. The erythrocytes rose from 3,200,000 to 4,160,000; the hemoglobin from 30 to 55 per cent. The child was taken from the hospital to return in seven months, at which time the red blood cells numbered 3,702,000 and the hemoglobin 45 per cent. As this blood count was made after hemorrhages from the intestines, it gives no information as to whether the increasing anemia was due to losses of blood or whether it was evidence of persistent blood destruction associated with the disease itself.

Independent of this case, it is important that, following repeated transfusions, improvement in an anemia is only temporary. The interpretation of a transitory improvement in the blood is that the agent determining blood destruction is dominant. Consequently, a combination of persistent blood destruction and of an enlarged spleen in spite of repeated transfusions furnishes a good starting point for serious consideration of splenectomy.

It is desirable that a thorough search for evidence of blood regeneration as well as of blood destruction be made when one is confronted with the problem of splenectomy.

Evidences of	
Blood Destruction	Blood Regeneration
Polychromatophilia	Increased erythrocyte count
Microcytes	Increase of percentage of hemoglobin
Poikilocytes	Following transfusion an increase in reticulated red cells; Howell-Jolly bodies; Cabot ring forms
Diminished blood platelets	
Leukopenia	
Increased urobilin in urine and stools	Blood platelets normal or increased.

The successive blood counts made after splenectomy in both cases are recorded in their respective charts. The erythrocytes steadily increased in number in both children. T. M. (Case 1) showed a count of 5,192,000 six months after the splenectomy. The hemoglobin was also increased but not in like degree. In both children, however, the hemoglobin may be regarded as within normal limits for their age

A leukocytosis followed the splenectomy in both cases. This is the usual reaction following splenectomy and indicates a favorable response of the blood forming organs. The later leukocyte counts correspond to the normal for children of their age.

Studies of the blood after splenectomy furnish a good index of the degree of improvement in the condition for the relief or cure of which the spleen was removed.

Hemorrhages.—T. M. (Case 1), had his first hemorrhage at 2½ years of age. The blood was evacuated by way of the rectum. "Bleeding from the rectum" was repeated several times during the following three years. He first vomited blood when he was 3½ years old. This was repeated twice in the following two years.

The repetition of hemorrhages, the persistence of anemia, in spite of transfusion, and the failure of radium to reduce the size of the spleen, were the chief reasons for deciding to do a splenectomy. Hemorrhages may, of course, occur from other mucous membranes than those of the gastro-intestinal tract. The occurrence of hemorrhages indicates that the pathologic process has involved tissues outside of the spleen. It is unfortunate to delay splenectomy until such a startling warning occurs. The proper time for the removal of the spleen is, therefore, in the early stages of the disease.

> Splenectomy in the first stage (Banti's disease) is not only accompanied by a lower mortality but in the great majority of cases has caused great and lasting improvement in the system, often amounting to a complete cure. When the third stage is reached, with permanent changes in the liver and circulatory system, not only is the operation most dangerous, but the chances for improvement are greatly lessened. . . . Nevertheless, the prevalent opinion is probably correct that the improvement that follows splenectomy in the early Banti's disease, in the great majority of cases, either amounts to a complete cure or persists without relapse for many years. Even in the third stage, splenectomy may be of value (Krumbhaar[1]).

Ascites.—T. R. (Case 2) presents an accumulation of fluid in the abdomen as evidence of an advanced stage of Banti's disease. The swelling in the abdomen, which was noted when she was between 3 and 4 years of age, was probably due to the fluid. About five and a half years later the abdomen was tapped and fluid drawn. This procedure was followed within a month by an exploratory laparotomy which disclosed a much enlarged spleen and a large amount of fluid in the abdomen. Two months later the spleen was removed. Three and a half years after splenectomy there was no evidence of fluid and no return of anemia. As stated above this case offers evidence of the improvement following splenectomy in the late stages of Banti's disease.

It is important, however, to remove the spleen in the early stages of the disease. An early splenectomy may prevent or postpone the

advanced pathologic changes of which hemorrhages and ascites are manifestations. Splenectomy should not be delayed until hemorrhages and ascites appear.

RESULTS OF TREATMENT: *Radium.*—The repeated treatments by radium of the enlarged spleen in the case of T. M. (Case 1), were of no help. The spleen was not reduced in size and the hemorrhages were not checked. At present it may be said that radium treatment has been of no avail in the treatment of Banti's disease.

Blood Transfusion.—The results of the transfusion of blood offer most important information in forming an opinion as to whether or not a splenectomy should be done. The assistance which blood transfusion offers in the problem under discussion may be stated as follows: If an infant or child has an enlarged spleen with a blood picture of secondary anemia and with evidence of blood destruction and if he receives two or more blood transfusions at intervals of a month without improvement in the blood condition, such an infant or child becomes the potential subject of a splenectomy.

Reference has already been made to the importance of excluding leukemia as a cause of an enlarged spleen. The typical forms of leukemia present little difficulty. It often requires serious study to exclude atypical forms of the disease. The determination of malaria, syphilis and tuberculosis as a cause of splenic enlargement offers less difficulty. A splenectomy in these diseases is contraindicated. If leukemia, malaria, syphilis, etc. (Chart 2), can be excluded, the indications for splenectomy under the conditions stated above, become definite.

The following case of Gaucher's disease furnishes no added criteria to assist one in a decision to do a splenectomy. The chief point of interest in this condition is that the spleen may attain a size greater than that of any of the diseases to which a splenectomy is applicable. As the pathologic condition probably develops simultaneously in the spleen, bone marrow, lymph nodes and elsewhere, there is little hope for permanent relief of symptoms. The operation has, however, been accompanied by temporary relief of symptoms. It must be remembered that a definite diagnosis of Gaucher's disease is almost impossible. The enlarged spleen and anemia, and the failure to secure permanent improvement by transfusion are sufficient criteria for removal of the spleen, assuming that definite causes for the splenic enlargement have been excluded. If one waits to give a definite name, e. g., Banti's disease, Gaucher's disease, to the condition to which an enlarged spleen is associated, there will be no occasion for splenectomy.

CASE 3.—The details of this case were supplied by Dr. William Downes from his service at St. Luke's Hospital, New York. G. B., 6 years of age, was admitted to St. Luke's Hospital July 26, 1919.

Chief Complaint.—Enlarged spleen.

Family History.—Negative.

Birth History.—Full term; normal delivery.

Previous Illnesses.—Has had measles, mumps, and pertussis. No other illness.

Present Illness.—When patient was about 1 year old the mother first noticed a lump in the left side under the ribs. A physician pronounced it a large spleen and said the child would "grow with it." Since then the spleen has increased in size until it fills the abdomen. Mother thinks patient's arms and legs have gotten thinner of late. No loss of weight. Once in two or three months patient has nose-bleed, which usually occurs during sleep. Mother does not think more than a teaspoonful or so of blood is lost. Bleeding stops very readily.

Physical Examination.—General appearance was that of a well nourished child of 6 years, not acutely ill. Only very slight adenitis.

Lungs and Heart: Apparently normal.

Abdomen: Liver very much enlarged. Absolute dulness to the fifth rib posteriorly and sixth rib anteriorly. Lower margin 3½ inches below the costal margin in nipple line. The spleen extends from the rib margin to the pubes on left side. In the right side the edge of the spleen is 2½ inches from the right anterior superior spine of the ilium.

July 26: One hundred and twenty mg. radium in 2 mm. lead and 3 cm. gauze to anterior and lower portion of the spleen for six hours.

August 2: One hundred mg. radium (as above) to left side of spleen for six hours.

August 30: One hundred and thirty mg. radium to upper anterior surface of spleen for six hours.

September 8: One hundred and thirty mg. radium in 2 mm. lead and 2 cm. gauze to side of spleen for six hours.

October 10: One hundred and thirty mg. radium applied to each of four areas of spleen for six hours.

October 12: Patient was discharged with condition practically unchanged.

Nov. 3, 1920: Patient was readmitted on this date. Since last admission patient has had occasional slight hemorrhages from the nose but felt in usual health and gained 2½ pounds. Appetite was fair. Seven weeks ago went to school; when she returned she complained of pain in left side of abdomen so went to bed. Magnesia was prescribed and bowels moved with relief. The next night had a severe hemorrhage from nose; this was repeated the next day and the doctor was called. The nose was plugged and the hemorrhage stopped. Since then she has had a weekly recurrence of hemorrhage, some severe. Thromboplastin usually stopped the hemorrhage. She was able to walk around while at home, and except for occasional headache had had no complaint.

Physical Examination.—General appearance was that of a poorly nourished, underdeveloped, and anemic white girl. Expression dull but mentally bright and observant. Face is pale. Lips and nostrils show dried blood evidently from recent hemorrhage. Neck: There is a marked bilateral systolic pulsation seen. There is a large palpable cord seen on the left side of the neck not pulsating and not tender. A few enlarged glands felt at angles of the jaw. Thorax: Measures 59 cm. in circumference at level of nipples. Marked emaciation with prominent external mammary veins anastomosing below the superficial epigrastric veins. Lower part of thorax flares markedly and yet is symmetrical. Lungs: Apex beat felt fourth space in recumbent position, 7 cm. to left of midsternal line. No thrill palpable. At apex, sounds are loud and rough and valvular. There is a short, low systolic murmur heard best at junction of fourth left rib with sternum, but also over apex, but not trans-

mitted to axilla. At base, systolic murmur heard over aortic and pulmonic areas transmitted to neck. Pulse rate 134, regular, poor volume, well sustained and of good force.

Abdomen: Measures 70.5 cm. at level of umbilicus, very prominent; skin pale, veins prominent. Liver extends 8 cm. below costal arch in right mammary line. Spleen extends 7 cm. to right of umbilicus and down into pelvis.

November 6: Blood transfusion given; 13 ounces of citrated whole blood.

November 9: Condition about the same. Patient had slight bleeding from the nose last night.

November 15: Patient was transferred to surgical service. Age, 7 years.

Diagnosis.—Splenic anemia.

Treatment.—November 16: Operation, splenectomy. Operator, Dr. William Downes. Patient died the same day.

Pathologic Findings at Operation.—The spleen was enormously enlarged, being nearly the size but not the contour of the average adult liver; it was mottled with dark purplish spots, somewhat scarred looking areas. It was adherent to the stomach and liver at its upper pole. On its upper and outer surface was an area 4 by 6 inches yellowish, soft, necrotic, and partially broken down in the form of an abscess. The veins of the hilus of the spleen were enormously dilated.

TABLE 5.—RESULT OF BLOOD EXAMINATIONS IN CASE 3

Date	Erythrocytes	Hemoglobin, per Cent.	Leukocytes	Polymorphonuclears, per Cent.	Lymphocytes, per Cent.	Remarks
7/26/19	2,100,000	50	4,000	38	62	Moderate anisocytosis and poikilocytosis; one normoblast seen
8/ 8/19	.....	..	8,700	60	40	Anisocytosis, poikilocytosis, polychromatophilia, Howell-Jolly bodies
10/ 3/20	840,000	19	2,800	75	24	Patient readmitted, having been at home over a year
10/ 6/20	740,000	17				
10/ 6/20	.....	..	Transfusion	..	..	13 oz. citrated whole blood given intravenously
10/ 7/20	2,000,000	30	2,000	78	32	
10/ 9/20	1,100,000	24	.....	..	..	Slight bleeding from nose last night; condition about same
10/10/20	.....	24				
10/12/20	1,100,000	25				
10/14/20	.....	..	Transfusion	..	..	300 c.c. of citrated whole blood given intravenously
10/16/20	.....	..	Splenectomy	..	..	Died same day

Operative Procedure.—Peritoneal cavity opened and the pathology of the spleen noted; it was free from adhesions to the liver and stomach. An opening was made into the abscess over the necrosed portion; pus and necrotic material were aspirated. The lower lobe of the spleen delivered out of the wound, the vessels at the hilus clamped and the organ excised.

Urine Examination.—Nov. 3, 1919: negative.

Pirquet test not made.

Wassermann: Aug. 8, 1919, negative.

Blood for grouping, Nov. 3, 1920, Group III.

REPORT OF PATHOLOGIC EXAMINATION OF THE SPLEEN

Macroscopic Examination.—Specimen consists of a spleen measuring 30x16x9 cm. and weighing 1900 gm. The capsule is smooth, except over one or two small areas on the inferior surface overlying a large area of infarcation. The latter crosses the anterior surface forming a broad, irregular but sharply defined

yellow area from 6 to 8 cm. wide and penetrating into the substance from 2 to 5 cm. Other yellowish placques, smaller and ever more irregular, are found toward the upper pole. The vessels at the hilus are small and surrounded by about ten lymph nodes, all soft, dark red and resembling the spleen itself. Their capsules are thin and soft. On section it shows the uniform porphyry red color, all the normal markings being obliterated. The surface is smooth, cellular and dull without large vessels.

Microscopic Examination.—Sections of the spleen show no normal tissue, there being only a few flattened cords representing the original structure and a few fibrous trabeculae. The morphology is uniformly altered by the extreme dilation of the sinuses, which are distended to form rounded alveoli, lined with and partially filled with small eccentric rounded nuclei. These cells are rather granular, some of them distinctly pigmented with fine yellowish granules distributed throughout the cytoplasm uniformly.

Diagnosis.—Gaucher's disease.

It does not come within the scope of this paper to give an exposition of hemolytic jaundice. It is sufficient to state that of those conditions to which splenectomy appertains, hemolytic jaundice, familial or acquired, offers the greatest hope of a cure by removal of the spleen.

The problem in this disease, as far as it relates to splenectomy, is quite the same as in Banti's or Gaucher's disease. The decision to remove the spleen is based on the presence of a large spleen, persistence of a secondary anemia after repeated blood transfusions, and a physical disability which make the individual a chronic invalid. Hemolytic jaundice has the advantage of a distinguishing sign in the icterus. This is a great aid in stimulating interest in an explanation of the jaundice. If the term "Haemolytic jaundice" fits the condition, one is in a position to assert that splenectomy offers the best chance of curing the disease.

CONCLUSIONS

1. The conditions for which relief or cure by splenectomy may be indicated are present in the first years of life more frequently than is generally accepted.

2. It is desirable to remove a spleen in the early stages of the pathological process for which splenectomy is indicated.

3. Hemolytic jaundice presents the most favorable condition for cure by splenectomy.

4. Banti's disease and Gaucher's disease represent pathologic processes for which splenectomy may give relief of symptoms and may serve to prolong life.

5. Von Jaksch's disease is probably not an independent condition.

6. Indications for the removal of the spleen depend on certain criteria, not on the making of a definite diagnosis. These criteria are splenomegaly, secondary anemia, and the failure of repeated blood transfusions to determine any improvement in the anemia and general condition.

THE BACTERIOLOGY OF THE NORMAL INFANT'S URINE*

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It has been rather generally accepted that the urine of normal infants often contains a small number of organisms that cannot definitely be excluded as contaminations. The work of Ross,[1] Beeler and Helmholz,[2] Kleinschmidt,[3] and others substantiates this view. Recently the entire question was reopened by Langer and Soldin [4] who claim that all former work in which liquid mediums had not been used for the isolation of bacteria is open to criticism. In a series of 138 cases they isolated *Streptococcus lacticus* 128 times, *Bacillus coli* sixteen times, and *Bacillus lactis aerogenes* four times; *Bacillus coli* was associated with *Streptococcus lacticus* six times. Occasionally, a single examination revealed sterile urine, but on repetition bacteria were found. At that no account is taken of anaerobic bacteria.

Langer and Soldin speak only of washing the urethra thoroughly with a 10 per cent. boric acid solution. The solvent for the boric acid is not mentioned, and in a single sentence, without any citation of experiments, they consider all portions of the urine alike with regard to bacterial content and formed elements. The most striking features of their series are the constant presence of bacteria of the colon group and the complete absence of staphylococci which are normally present in the female urethra. This is in direct contrast to the findings of Beeler and Helmholz,[2] namely, that only exceptionally were bacilli of the colon group found, and when organisms were present they were usually staphylococci or diphtheroids. Kleinschmidt cultured, on solid

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1. Ross, A.: The Bacteriology of the Urinary Tract in Children, Lancet **1**:654, 1915.

2. Beeler, C. and Helmholz, H. F.: The Bacteriology of the Urine in Healthy Children and Those Suffering from Extra-urinary Infections, Am. J. Dis Child. **12**:345 (Oct.) 1916.

3. Kleinschmidt, H.: Zur Bakteriologie des Harns beim Säugling, Jahrb. f. Kinderh. **94**:77, 1921.

4. Langer, H. and Soldin, M.: Zur Aetiologie der Säuglingspyelitis, Ztschr. f. Kinderh. **19**:161, 1919.

mediums, fifty-four specimens of urine from female patients and obtained sterile urine in all but ten, while in liquid mediums he obtained bacteria in thirty-two of sixty-two cultures. Further, he says that he was rarely able to obtain the same flora in successive examinations, which he interprets as the result of varying contaminations. Dextrose bouillon yielded positive cultures more often than plain bouillon; the percentages, however, are not indicated. He isolated *Streptococcus lacticus* more often than any other organism; second in line are members of the colon group, third the staphylococci.

Inasmuch as the former work of one of us was carried on entirely on various solid mediums, it was thought wise to repeat the work, using also the liquid culture medium suggested by Langer and Soldin. This

TABLE 1.—RESULTS OF CULTURES

No.	Sex	Specimen 1		Specimen 2	
		Liquid Medium	Solid Medium	Liquid Medium	Sol d Medium
19	Boy	Bacillus subtilis	Negative	Negative	Negative
28	Girl	Negative	Negative	Staphylococcus	Negative
30	Boy	Negative	Negative	Gram-positive bacillus spore-former	Negative
31	Girl	Gram-negative streptococcus not identified	Negative	Negative	Negative
40	Boy	Gram-positive spore-former	Negative	Negative	Negative
80	Girl	Gram-positive diplococcus not Streptococcus lacticus	Negative	Negative	Negative
10*	Boy	Gram-positive staphylococcus after one week	Negative		
32*	Girl	Gram-negative bacillus short, Bacillus subtilis	Negative		
33*	Boy	Staphylococcus	Negative		
34*	Girl	Bacillus subtilis	Negative		
77*	Boy	Gram-positive staphylococcus	Negative		

* One specimen only was obtained.

seemed the more important as the constant presence of *Streptococcus lacticus* in the normal urine would be of great importance in settling the problem of the mode of infection in pyelitis.

The infants from whom the urine was taken for this study ranged in age from 6 weeks to 16 months. All had normal temperatures and were normal or nearly normal in weight. All were free from any infection or disease, as indicated by physical examination. Some of the infants were entirely breast fed, others were breast and bottle fed, and still others were fed entirely with artificial food.

The technic of obtaining urine was practically the same as that described by Beeler and Helmholz. The catheters used were of metal, varying from 1.5 to 2.5 mm. in diameter, with a short rubber tube attached by means of which the flow of urine could be controlled and collected in two separate tubes. The catheters were sterilized indi-

vidually in large test tubes so that they could be removed without danger of contamination.

To catheterize a patient three persons were always at hand; one to hold the limbs of the child, one to separate the labia, cleanse the parts, and pass the catheter, and a third to play the stream of compound solution of cresol, pass out the catheter, and hold the test tubes to receive the urine.

The meatus was cleansed as follows: The labia were held apart or the foreskin was retracted and the debris loosened by a small sterile applicator, while a steady stream of 1 per cent. compound solution of

TABLE 2.—RESULTS OF CULTURES

No.	Sex	Specimen 1			Specimen 2		
		Liquid Medium	Solid Medium	Colonies in Each C.c.	Liquid Medium	Solid Medium	Colonies in Each C.c.
12	Girl	Negative.....	Negative.....	0	Staphylococcus	Staphylococcus	1,000
19	Boy	Bacillus subtilis	Negative.....	0	Negative.....	Negative.....	0
26	Boy	Negative.....	Negative.....	0	Bacillus subtilis	Bacillus subtilis	Countless
28	Girl	Negative.....	Negative.....	0	Staphylococcus	Negative.....	0
30	Boy	Negative.....	Negative.....	0	Gram-positive bacillus, spore-former	Negative.....	0
31	Girl	Streptococcus, not identified	Negative.....	0	Negative.....	Negative.....	0
40	Boy	Gram-positive bacillus, spore-former	Negative.....	0	Negative.....	Negative.....	0
48	Boy	Staphylococcus	Staphylococcus	1	Negative.....	Negative.....	0
78	Boy	Gram-positive staphylococcus and non-pathogenic bacillus	Gram-positive staphylococcus and non-pathogenic bacillus	4	Negative.....	Negative.....	0
80	Girl	Gram-positive diplococcus not S. lacticus	Negative.....	...	Negative.....	Negative.....	0

cresol was played on the region of the meatus. A dry sterile applicator was then applied directly over the meatus to remove any excess fluid. The catheter was then inserted. If there was enough urine in the bladder two specimens were collected.

The urine was cultured in tubes containing 1 per cent. dextrose broth titrated to a hydrogen ion concentration of from 7.6 to 7.8 on plates of litmus-lactose-agar, made by adding 1 per cent. agar, 1 per cent. lactose and 1 per cent. litmus to plain broth that had been titrated to p_H 7.6-7.8. About 1 c.c. of urine was used in about 8 c.c. of broth, and from 0.5 to 1 c.c. for the plating in litmus-lactose-agar. The number of colonies of bacteria indicated in Tables 2 and 3 represent the number of bacteria for each cubic centimeter of urine. All streptococci were subcultured in litmus milk for identification. *Streptococcus*

lacticus was identified by a method very kindly furnished us by Prof. E. G. Hastings of the University of Wisconsin. The identification is based on the fact that *Streptococcus lacticus* reduces the litmus before curdling the milk, and the other streptococci produce a pink curd in the milk without reducing the litmus.

Seventy infants, thirty-five girls and thirty-five boys, were studied. The findings can best be grouped under headings as follows:

1. *All Cultures Negative.*—In this group there were thirty infants, seventeen girls and thirteen boys. In only twenty-one of the thirty was it possible to obtain enough urine for two specimens. This group represents 40 per cent. of the samples examined and in two-thirds of these the sterility of the urine was determined in duplicate on Specimens 1 and 2. The cultures in cases in which two specimens were obtained are included in this group only when all four were sterile. In the others of this series one specimen only was obtained, and cultures were sterile in both liquid and solid mediums.

2. *Cultures in Solid Mediums Negative, in Liquid Mediums Positive.*—Much to our surprise, this group was relatively small, eleven cases (five girls and six boys). Langer and Soldin's work led us to believe that this would make up the largest group of the series. The various organisms in cultured liquid mediums are given in Table 1. The importance of this group is paramount in disproving Langer and Soldin's contention that liquid mediums are essential for this work. In only 15 per cent. has it made a difference, and even here the significance is doubtful.

3. *Cultures in Solid Mediums Positive, in Liquid Mediums Negative.*—Of the three cases in this group (two boys and one girl), contamination was unquestionable in two; in the third were two colonies of streptococci, which may or may not have been due to contamination.

4. *Cultures of One Specimen Positive, and All Cultures from the Other Specimen Negative.*—Specimens 1 and 2 refer to the first and second portions of urine obtained by catheterization. There were ten cases in the group (six boys and four girls, Table 2). Contrary to expectation Specimen 1 was sterile four times and Specimen 2 showed growth six times, indicating that the first portion of the urine voided does not necessarily contain the contaminating bacteria. In only two of the four was there growth in the solid mediums inoculated from Specimen 2.

5. *All Cultures Positive.*—In most of the twenty-six cases in this group (fourteen boys and twelve girls), all the cultures showed growth although occasionally one or another was negative. The num-

TABLE 3.—RESULTS OF CULTURES

No.	Sex	Specimen 1			Specimen 2		
		Liquid Medium	Solid Medium	Colonies in Each C.c.	Liquid Medium	Solid Medium	Colonies in Each C.c.
2	Girl	Negative.....	Negative.....	0	Gram-positive staphylococcus, large	Gram-positive staphylococcus, large	1,000
5	Girl	Gram-positive streptococcus not identified	Gram-positive staphylococcus, large	920			
6	Girl	Gram-positive streptococcus not identified, gram-negative bacillus non-pathogenic	Gram-negative streptococcus not identified, gram-negative bacillus, gram-negative staphylococcus	570			
8	Girl	Gram-negative bacillus probably B. coli, gram positive streptococcus not identified	Gram-negative bacillus probably B. coli	800			
22	Boy	Gram-positive streptococcus and Streptococcus lacticus	Bacillus coli	130	Gram-positive streptococcus and Streptococcus lacticus		
25	Boy	Gram-positive staphylococcus, large	Gram-positive staphylococcus, large	6			
36	Boy	Staphylococcus	.....	...	Staphylococcus	Staphylococcus	38
37	Boy	Staphylococcus, large	Staphylococcus, large	2	Staphylococcus, large	Staphylococcus, large	26
42	Girl	Gram-positive staphylococcus, large, and S. lacticus	Staphylococcus and B. subtilis	20	Gram-positive staphylococcus, large, and S. lacticus	Staphylococcus, B. subtilis, and one colony of S. lacticus	8
44	Girl	.....	.....	...	Streptococcus, not S. lacticus	Streptococcus, not S. lacticus	Few
45	Girl	Streptococcus lacticus and diplococcus	.....	...	Streptococcus lacticus and diplococcus	Streptococcus lacticus and diplococcus	6
47	Girl	Gram-positive staphylococcus	Gram-positive staphylococcus	2	Gram-positive staphylococcus	Negative.....	0
48	Boy	Gram-positive staphylococcus	Gram-positive staphylococcus	1	Negative.....	Negative.....	0
53	Girl	Gram-negative bacillus not B. coli and gram-positive staphylococcus	Gram-negative bacillus not B. coli	2			
54	Boy	Gram-positive staphylococcus, large	Staphylococcus, large	58	Few staphylococci, large	Negative.....	0
56	Boy	Gram-negative staphylococcus	Staphylococcus	100	Staphylococcus	Staphylococcus	100
59	Boy	Staphylococcus, large	.....	...	Staphylococcus, large	Staphylococcus, large	50
60	Boy	Gram-positive staphylococcus, large	Staphylococcus, large	6	Streptococcus, not S. lacticus		
61	Boy	Staphylococcus, large	Staphylococcus, large	15	Staphylococcus, large		
64	Girl	Streptococcus lacticus and gram-negative spore-former	Staphylococcus, large and Streptococcus lacticus	3			
67	Boy	Gram-negative staphylococcus	Bacillus subtilis	1			

TABLE 3.—Results of Cultures—(*Continued*)

No.	Sex	Specimen 1			Specimen 2		
		Liquid Medium	Solid Medium	Colonies in Each C.c.	Liquid Medium	Solid Medium	Colonies in Each C.c.
74	Girl	Staphylococcus, large and spore-forming bacillus	Staphylococcus, large and spore-forming bacillus	3	Staphylococcus, large		
75	Boy	Staphylococcus, large	Spore forming bacillus	10	Spore-forming bacillus		
76	Boy	Gram-negative bacillus, non-pathogenic	Gram-negative bacillus, non-pathogenic	2	Gram-negative bacillus, non-pathogenic	Negative.....	0
81	Boy	Negative.....	Bacillus coli and Streptococcus lacticus	4	Streptococcus lacticus and Bacillus coli	Streptococcus lacticus and Bacillus coli	200
82	Boy	Negative.....	Staphylococcus, large	1	Gram-negative bacillus, spore-former	Negative.....	0
83	Girl	Staphylococcus, large	Staphylococcus, large	10	Staphylococcus, large, and streptococcus not identified	Staphylococcus, large	6
85	Girl	Two streptococci, one S. lacticus	Negative.....	0	Two streptococci, one S. lacticus	Two streptococci, one S. lacticus	Many

ber of bacteria for each cubic centimeter is of interest in that in only six cases were there 100 or more organisms for each cubic centimeter of urine. In eight cases there were from ten to 100 organisms for each cubic centimeter, and in twelve there were less than ten. In Table 3 the results of the cultures in this group are given in detail.

In fourteen instances streptococci were isolated from the urine; in six the organism was definitely identified as the *Streptococcus lacticus,* in five it was not definitely identified, and in three it was definitely not *Streptococcus lacticus.* Thus of seventy specimens of urine *Streptococcus lacticus* was possibly present in eleven, and definitely absent in fifty-nine (84.28 per cent).

DISCUSSION

The results of our studies emphasize again the futility of obtaining evidence by the method of Langer and Soldin that in any way will help to settle the problem of the mode of infection in pyelitis. The error that creeps in by contamination, even when all precautions are taken, is such that the evidence obtained is always open to criticism. Our data show that in three-sevenths of the specimens examined the urine was sterile; in two-thirds of these the determination was made in duplicate. We cannot agree with Kleinschmidt that at each catheterization a different flora is obtained, nor with Langer and Soldin that a sterile specimen is only an accident, and repeated catheterization will always yield

bacteria in the urine. We have recatheterized repeatedly and obtained identical results both with regard to sterility and flora. Furthermore, we wish to call attention to types of organisms constantly found by Kleinschmidt and by Langer and Soldin, namely, those of the colon group and *Streptococcus lacticus,* all inhabitants of the intestinal canal and so far as we know not present normally in the urethra. Kleinschmidt asserts that by taking smears from the meatus after cleansing it he was able to prove the constant presence of an organism of the same type as that found in his cultures of the urine. The method used by Langer and Soldin of obtaining cultures is also open to criticism since by washing out the urethra, organisms may easily be washed into the bladder. Langer and Soldin found long chains of streptococci, as shown in one of their illustrations. These they believe have grown from organisms coming from the kidney. The more plausible interpretation is that they are washed in from the urethral opening and are essentially contaminations, as it is not likely that organisms would grow so rapidly in the urine and not grow in more favorable culture mediums after inoculation. Our findings are further at variance with those of Kleinschmidt and of Langer and Soldin in the frequency of occurrence of the *Streptococcus lacticus,* which was almost omnipresent in their cultures. The *Streptococcus lacticus* was definitely identified in only six instances, it may have been present in five others, so that at most it was present in 15 per cent. of the urines examined. In six of eleven instances the *Streptococcus lacticus* was found in the liquid medium and not recovered on the solid medium.

CONCLUSIONS

1. The urine of infants is sterile on culture in from one-third to one-half of the experiments.

2. *Streptococcus lacticus* is only exceptionally found in the urine of infants.

3. The chances of contamination are so great that the presence of organisms in the urine does not prove, without further control, that they have come from the kidney.

THE VALUE OF CUTANEOUS SENSITIZATION TESTS EMPLOYED IN ECZEMA AND PAPULAR URTICARIA OF CHILDHOOD*

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In this discussion, we are not concerned with the controversy as to whether the cutaneous sensitization observed clinically in eczema, urticaria papulosa and angioneurotic edema in infants and children is a phenomenon of anaphylaxis or a state of allergy. We believe that the question will be settled when the mechanism of protein sensitization is more definitely known. However, the fact remains that local cutaneous reactions are brought to light when various proteins are applied by cutaneous or intracutaneous tests to the skin of patients who are subjects of the diseases mentioned. The results indicate that these cutaneous reactions depend on a protein substance which is the essential cause of the efflorescence in a comparatively large number of cases. Moreover, the cause of the disease having been determined, with intelligent cooperation on the part of the parents of the patient in regard to diet, the clinical cure far surpasses the results of any other mode of treatment.

The application of cutaneous sensitization tests in cases of dermatitis in adults in which a protein may be suspected as a possible cause has been a routine practice of late in the Dermatological Dispensary of the Jefferson Medical College Hospital. The favorable results derived from the practice prompted us to apply protein sensitization tests to children having eczema and urticaria.

Pirquet [1] was the first to suggest a method for determining cutaneous sensitization to proteins, but it remained for Schloss to make clinical application of the procedure in children. Schloss' [2] patient was a boy, 8 years of age, who was subject to marked urticarial lesions caused by the ingestion of eggs, oatmeal and almonds. The patient's history suggested that the urticaria subsequent to the ingestion of these foods was not a congenital condition but was acquired during early life. It was found that the cutaneous reaction was produced only by the protein constituent of egg, almonds and oats. During the time the

* Received for publication Nov. 21, 1921.
* From the Department of Dermatology, Jefferson Medical College.
1. Pirquet, C.: Arch. Int. Med. **7**:259 (March) 1911.
2. Schloss, O. M.: Am. J. Dis. Child. **3**:341 (May) 1912.

patient was on a diet free from these substances, he was also free from urticarial attacks. Schloss succeeded eventually in immunizing this boy by feeding him gradually increasing doses of the protein constituent of eggs. Blackfan [3] found evidence of susceptibility to protein in twenty-two out of twenty-seven patients with eczema whom he tested intracutaneously. When his patients were placed on a diet free from or limited in animal proteins, the eczema was markedly improved in each case. Engman and Wander [4] found that in their series 78 per cent. of children with eczema are sensitized to some protein. In the cases in which the patients' parents cooperated with them, the results were "brilliant." In our own series, the percentage of positive sensitization and the general results compare favorably with those of Blackfan, Engman and Wander.

From our own work on adults, we found that the intracutaneous method is more sensitive and subject to fewer errors than the cutaneous method. It is not possible to make a series of abrasions that exactly correspond in length and depth. It is impossible to apply the same amount of powdered protein substance to the abrasion, unless previously weighed—an almost impossible and certainly impractical undertaking, especially when one is called on to make a large number of tests. On the other hand, when the intracutaneous method is employed, the solution containing the protein can be standardized. The standardization depends on the percentage of nitrogen in each protein determined by the Kjeldahl method. Having standardized the solution, the exact amount to be injected can be measured out by an accurate syringe. In our investigation we employed the commercial product throughout. We had occasion to compare the end-results of tests with the commercial proteins with those performed with a number of protein substances that we ourselves had prepared according to the method of Wodehouse and Olmstead.[5] The results were found to be identical.

The protein test substance is dissolved in physiologic solution of sodium chlorid and the usual amount of phenol was added as a preservative. The solution is then tested for sterility. The skin of the arm is cleansed, and 0.05 c.c. of the desired test protein is injected intracutaneously. A successful injection is followed immediately by the appearance at the site of the injection of a raised white spot resembling a wheal. More than one control, consisting of the menstrum, is used.

The cutaneous reaction may be immediate or delayed for forty-eight hours. The appearances necessary to establish a positive immediate

3. Blackfan, K. D.: Am. J. Dis. Child. **11**:441, 1916.
4. Engman, M., Jr., and Wander, W. G.: Arch. Dermat. & Syph. **3**:223 (March) 1921.
5. Wodehouse, R. P., and Olmstead, J. M. D.: Boston M. & S. J. **176**:467, 1917, ibid. **177**:85, 1917.

test are a wheal and a red areola surrounding the wheal. The criteria for a delayed positive test are a papular induration and an erythema persisting for forty-eight hours. The intensity of the reaction is determined by reading the tests against the controls. If the wheal or papule equals the control and presents no erythema, it is negative; if it is half again as large and surrounded by erythema, it is +; if twice as large, it is + +, and so on.

Twenty-three infants and children with eczema were tested. Eight, or 35 per cent., gave negative reactions. Fifteen, or 65 per cent., had one or more positive reactions. Six, or 40 per cent., of the fifteen patients were clinically cured; three patients, or 20 per cent., showed marked improvement; six, or 40 per cent., were improved.

Twelve children with papular urticaria were tested. Three, or 25 per cent., were negative as far as reactions were concerned. Nine, or 75 per cent., reacted to one or more proteins. Three of the nine cases were clinically cured; four were markedly improved. Of the two remaining children, one reacted to strawberry +, orange +, and banana +; the other one reacted to potatoes + and tomatoes +. Both children failed to improve on a restricted diet.

The cause and progress in several of the cases in our series are worthy of more detailed comment.

SUMMARY OF CASES

CASE 1 (Table 1).—H. S., aged 3 months, breast fed, had an eczema of the face. The child reacted to mother's milk +, cows' milk +. Elimination of the mother's and of the cows' milk failed to cure or improve the dermatosis.

CASE 2 (Case 4, Table 1).—M. K., aged 14 months, had an eczema of the face. The reaction to food proteins was positive for egg yolk, + +; egg white, + +, and oatmeal +. The patient was placed on a diet free from eggs and cereals, and during the first two weeks colonic irrigations were ordered. When last observed the eczema was very much improved.

CASE 3 (Case 8, Table 1).—H. L., aged 8 months, had had an eczema of the face for four months when first examined. He reacted to rice, + +, and barley, + +. He was given colonic irrigations of physiologic solution of sodium chlorid and a diet consisting of milk. After the eczema had been clinically cured, the patient was tested and again reacted to barley and rice.

CASE 4 (Case 12, Table 1).—J. C., aged 4 years, had a generalized papulovesicular eczema of two months' duration. The reaction to food proteins was positive for beef, + + +; lamb, + +, and peanuts, +. The elimination of all forms of meat from the diet resulted in a clinical cure.

CASE 5 (Case 5, Table 1).—This case serves as an illustration of how difficult it is at times to prove the pathogenesis of a suspected cause. P. S., aged 11 months, had an eczema of the face and an abscess of the left cheek. The reaction to food proteins was negative, but the response to the *Staphylococcus pyogenes* was + +. Surgical attention was first given the abscess. As it improved it was noticed that the eczema was improving. By the time the abscess had nearly healed, the eczema was practically well. When the patient was last seen the eczema had completely cleared up. The patient failed to react to food proteins but reacted to bacterial proteins. The eczema first

TABLE 1.—PROTEIN REACTION IN CASES OF ECZEMA; RESULTS OF TREATMENT

Case	Age	Distribution	Duration	Reaction	Result
1. H. S.	3 mos.	Face	1 mo	Mother's milk + Cows' milk +	No improvement
2. E. H.	10 mos.	Face	1 mo.	Potatoes ++ Herring ++	Improved
3. F. W. C. ...	3 yrs.	General	6 mos.	None	Unimproved
4. M. K.	14 mos.	Face	2 mos.	Egg yolk ++ Egg whites ++ Oatmeal +	Marked improvement
5. P. S.*	11 mos.	Face	2 wks.	Staphylococcus pyogenes ++	Clinical cure
6. M. S.	12 yrs.	Upper and lower extremities	11 mos.	None	Unimproved
7. S. G.	14 mos.	Lower extremities	2 mos.	None	Unimproved
8. H. L.	8 mos.	Face	4 mos.	Barley ++ Rice ++	Clinically cured
9. R. M.	16 mos.	Face	5 wks.	Rye + Egg yolk ++ Egg white ++	Clinically cured
10. M. E. T. ...	8 mos.	Face	2 wks.	Tuberculin ++++	Not improved
11. W. McK. ...	2 yrs.	General	21 mos.	Cheese +	Not improved
12. J. G.	4 yrs.	General	2 mos.	Beef +++ Lamb ++ Peanuts +	Clinically cured
13. N. P.	3 yrs.	General	21 mos.	Spinach ++	Improved markedly
14. G. M.	2 yrs.	Face	6 mos.	Egg white ++ Wheat ++	Improved
15. P. R.	19 mos.	Face	2 wks.	Oatmeal +++	Clinically cured
16. L. R.	3 yrs.	Upper extremities	4 wks.	Tomatoes +++	Clinically cured
17. J. R.	8 mos.	Upper extremities	4 mos.	None	Not improved
18. B. B.	14 mos.	Lower extremities	2 mos.	Wheat +++ Egg white ++ Potato + Rice +	Improved
19. W. T.	4 yrs.	General	1 yr.	Pork +++ Beef +++ Veal ++	Marked improvement
20. E. B.	2 yrs.	Face	2 wks.	Cheese + Beans ++ Coffee +	Improved
21. L. Z.	4 yrs.	Face	7 wks.	Tomatoes ++ Grape fruit ++ Peas ++	Improved
22. R. H.	5 yrs.	General	2 yrs.	Cod fish ++ String beans + Lima beans +	Improved
23. C. R.	2 yrs.	Face and hands	6 mos.	Milk + Veal +	Not improved

* This patient also had an abscess.

improved and later cleared up entirely following the surgical treatment of the abscess. Apparently the cause of the eczema in this case was a bacterial protein.

CASE 6 (Case 2, Table 2).—S. E., aged 6, had an urticarial eruption of three days duration. All sensitization tests were negative with the exception of cucumber + +. Treatment consisted of colonic irrigation and an antipruritic lotion locally. The patient has been under observation for six months without a recurrence of urticarial lesions.

CASE 7 (Case 6, Table 2).—W. S., aged 3 years (a private patient) had a papular urticaria involving the face and extremities. Herring gave a + + reaction. The tests were made following the second attack, when it was found that herring was responsible. The mother of the patient volunteered the information that the child had been given anchovies thirty-six hours before the last attack, and that the patient had had anchovies for the first time in May, 1921. The third attack was brought about deliberately.

TABLE 2.—PROTEIN REACTION IN CASES OF PAPULAR URTICARIA; RESULTS OF TREATMENT

Case	Age	Distribution	Duration	Reaction	Result
1. J. H.	7 yrs.	Upper and lower extremities	2 yrs.	Negative	Unimproved
2. S. E.	6 yrs.	Upper and lower extremities	3 days	Cucumber ++	Clinically cured
3. C. H.	18 mos.	Upper and lower extremities	6 mos.	Oats ++ Veal ++	Improved
4. S. K.	3 yrs.	General	10 days	Chicken ++++	Clinically cured
5. G. P.	7 yrs.	General	2 yrs.	Strawberry + Orange + Banana +	Not improved
6. W. S.	3 yrs.	Upper and lower extremities and face	5 mos.	Herring ++	Clinically cured
7. J. H.	7 yrs	General	18 mos.	Beef ++ Egg yolk +++ Egg white +++ Oats ++	Much improved
8. W. T.	3 yrs.	Upper and lower extremities	1 yr.	Milk +++	Improved
9. I. G.	4 yrs.	Upper and lower extremities	1 yr.	Potato + Cows' milk ++ Egg white +++ Wheat +++	Improved
10. I. G.	18 mos.	Extremities	1 mo.	Negative	No improvement
11. E. M.	2 yrs.	Face	2 mos.	Negative	No improvement
12. L. P.	3 yrs.	Lower extremities	1 yr.	Potatoes + Tomatoes +	No improvement

CASE 8 (Case 8, Table 2).—W. T., aged 3 years, was affected with papular urticaria of one year's duration. A positive reaction to a food protein was obtained with milk + + +. Colonic irrigations, alkalies and phenyl salicylate by mouth and elimination of all dairy products from the diet gave an excellent result. At the end of nine days the patient was free from urticarial lesions. Three days later his mother gave him ice cream and the urticaria reappeared the same day.

CASE 9 (Case 9, Table 2).—I. G., aged 4 years, has had a generalized urticarial eruption for the past twelve months. The reaction to food proteins

was: beef + +, egg yolk + +, egg white + +, wheat + + +. That the urticaria was only improved, we believe, is due to the fact that the cooperation on the part of the mother in regard to diet was not entirely satisfactory.

Reaction to more than one protein in the same patient is a common occurrence. Reactions to test proteins which apparently have not entered into the diet of the patient have also been recorded. Also nonprotein substances, such as apothesin, quinin [6] and procain [7] have been found to cause skin reactions. The explanation of these apparent inconsistencies is to be found in the work of Schloss,[2] Wells and Osborne.[8] Schloss has pointed out the importance of recognizing that many foods are biologically related. Wells and Osborne, from their extensive investigations, concluded that the chemical structure rather than the biologic origin of the proteins determines the specificity of the anaphylactic reaction. How nonprotein substances operate to cause skin reactions has not been answered as yet. It has been suggested that chemicals like arsenic, quinin and other substances form compounds and alter the proteins of the body in a manner so as to form foreign proteins. Experimental evidence is lacking.

A factor that precludes a greater number of clinical cures in infants and children with eczema and papular urticaria associated with positive reactions to proteins, is the condition of the gastro-intestinal tract of these patients. Lack of unanimity exists among investigators in regard to permeability of undigested proteins when the alimentary epithelium is intact, but all agree that anatomic or functional abnormalities of the gastro-intestinal tract permit unaltered proteins to pass into the blood stream through the gastro-intestinal wall. Schloss and Worthen [9] found, by applying the precipitin test to the urine in atrophic infants with gastro-intestinal disorder, that unaltered proteins were absorbed through the walls of the intestine. Lust,[10] Modegliani and Benini [11] found that nutritional disorders favor the absorption of undigested proteins in children. Myehofer and Pribam [12] found that enteritis increases the permeability of the intestinal wall to crystalloids and colloids. Barnathan [13] states that disturbances in the gastro-intestinal tract interfering with the proper function of the digestive enzymes favor alimentary sensitization.

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10. Lust: Jahrb. f. Kinderh. **77**:244 and 283, 1913.
11. Modegliani, E., and Benini, R.: Policlinico **21**:540 (Dec. 20) 1914; Abst. J. A. M. A. **64**:476 (Jan. 30) 1915.
12. Myehofer and Pribam, E.: Wien. klin. Wchnschr. **22**:875, 1909.
13. Barnathan: Quoted by Highman, W. G., and Michael, J. C.: Arch. Dermat. & Syph. **2**:531 (Nov.) 1920.

From the preceding it may be inferred that proteins biologically related or chemically similar to an offending protein, though the latter may have been omitted from the patient's diet, may continue to cause the dermatosis. The condition of the gastro-intestinal tract may favor or inhibit the absorption of unaltered proteins to which the patient is sensitized and thereby either preclude the possibility of a clinical cure or help to increase the number of clinical cures.

SUMMARY

1. We have limited ourselves to the value of protein sensitization tests in children with eczema and papular urticaria.

2. The protein sensitization test proved of considerable value in ascertaining the etiologic factor in a fair number of cases of eczema and papular urticaria.

3. The elimination of specific offending proteins will not affect a cure in all cases of eczema or urticaria in children.

4. To be of value the food test must be + + or greater.

5. We may assume, that by correcting the gastro-intestinal abnormalities, an increase in the number of clinical cures is certain of attainment.

STUDIES OF INFANT FEEDING. XVII. A BACTERIO-CHEMICAL STUDY OF THE ACID STOOLS EXCRETED BY BREAST-FED AND BOTTLE-FED INFANTS*.

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BOSTON

It has been our experience to find that the stools from all babies receiving breast milk give an acid or neutral reaction when tested with litmus and that the stools from bottle-fed babies receiving simple cow's milk mixtures may be acid, neutral or alkaline when so tested. It has also been our experience to note that excoriation of the buttocks may often be associated with the elimination of acid stools.

The cause of the acid stools from bottle-fed babies has been a question of much theory and conjecture and up to the present time has not received any satisfactory explanation. It is our belief that the reaction of the stools may be dependent, to a great extent, on the chemical composition of the food ingested; that the composition of the food influences the bacterial growth within the intestines and determines the predominance of bacterial types; and that the type of bacteria present may account for the nature of some of the substances found in the feces.

This investigation was undertaken in order to learn something about the nature and cause of the acid stools eliminated by infants and involves both bacteriologic and chemical examinations of such stools. In this connection we have made determinations of the water soluble acidity and the total volatile acid content of twenty-four hour amounts of feces, the feces being marked by the use of carmine red. The nature of the volatile acid has also been investigated.

When this investigation was started we adopted the customary procedure of steam distillation for separating the volatile soluble fatty acids from the feces. We acidified with sulphuric acid and did not carefully control the volume of liquid in the distilling flask. We generally allowed the contents of the flask to concentrate as the distillation proceeded. This method was satisfactory in much of our work, especially on bacterial growths where little organic matter other

* Received for publication, Dec. 8, 1921.
* This investigation was conducted in the Boston Floating Hospital Laboratories.

than the fatty acids was present. It was customary to distill until a distillate neutral to litmus was given off.

When we began distilling stools from breast fed babies we noticed that the distillation continued to yield an acid distillate for a much longer period than had the previous materials. We concluded that the sulphuric acid must be decomposing some of the organic matter present, yielding volatile fatty acids, and thus prolonging the distillation indefinitely. To eliminate this possibility we so modified our technic as to eliminate all insoluble material from the distilling flask, and we acidified the material with phosphoric acid instead of sulphuric acid. This materially improved the method, but the distillate still continued acid for a greater volume than we had noticed before. Finally, we decided to investigate the nature of the fatty acids and we adopted the general method described by Dyer.[1] The large volume necessary to drive over all the fatty acids indicated the presence of formic acid. This observation was confirmed by qualitative tests. It became apparent that in the stools from breast fed babies we were for the first time encountering formic acid.

Dyer has shown that the distillation of volatile fatty acids at constant volume proceeds with a certain regularity and that the titration figures, when plotted as percentages on logarithmic coordinate paper, give a straight line for any individual fatty acid, and for a mixture of fatty acids a curve of variable shape, depending upon the particular fatty acids present in the mixture. By distilling pure acids in the apparatus used, the standard lines for these individual acids may be plotted as guides in the examination of mixtures. In order to determine the nature of the fatty acids in an unknown mixture we plotted the curve obtained from the distillation and compared this with the standard curves for pure acids.

As our study of the acid stools progressed we noted that the volatile acids we were dealing with were acetic and formic acids. We have therefore obtained the distillation figures and plotted the curves for pure acetic acid, pure formic acid and a mixture of equimolecular parts of the two acids. These distillation figures are given in Table 1 and the curves obtained are shown in Figure 1.

In plotting our curves we found that in every case our lines curved slightly to the left at the higher values. Dyer found that pure individual acids gave straight lines. The reason for this slight deviation was that our technic had for convenience been standardized with an assumed total titration rather than by carrying the titration to the true limit; that is, we distilled until the titration value of the 100 c.c. portion was less than 0.2 c.c. of tenth normal alkali. The sum of all titrations to this point was called the total titration. Since we were distilling a mixture of fatty acids we could not use Dyer's formula

1. Dyer: J. Biol. Chem. **28**:468, 1917.

TABLE 1.—Comparison of Rates of Distillation of Acetic Acid, Formic Acid and an Equimolecular Mixture of the Two Acids

Volume Distilled	Percentages Titrated		
	Acetic Acid	Acetic-Formic Mixture	Formic Acid
100	29.55	25.24	19.37
200	50.30	43.97	35.48
300	64.65	57.94	48.35
400	74.74	68.08	58.65
500	81.95	75.60	66.94
600	87.00	81.25	73.52
700	90.57	85.65	78.86
800	93.13	88.96	83.12
900	95.02	91.56	86.55
1000	96.37	93.57	89.30
1100	97.40	95.12	91.45
1200	98.07	96.36	93.17
1300	98.63	97.30	94.57
1400	99.00	98.00	95.70
1500	99.34	98.51	96.68
1600	99.53	98.92	97.50
1700	99.90	99.30	98.06
1800	100.00	99.60	98.57
1900	.....	99.93	98.97
2000	.....	100.00	99.34
2100	.....	.....	99.60
2200	.....	.....	99.84
2300	.....	.....	100.00

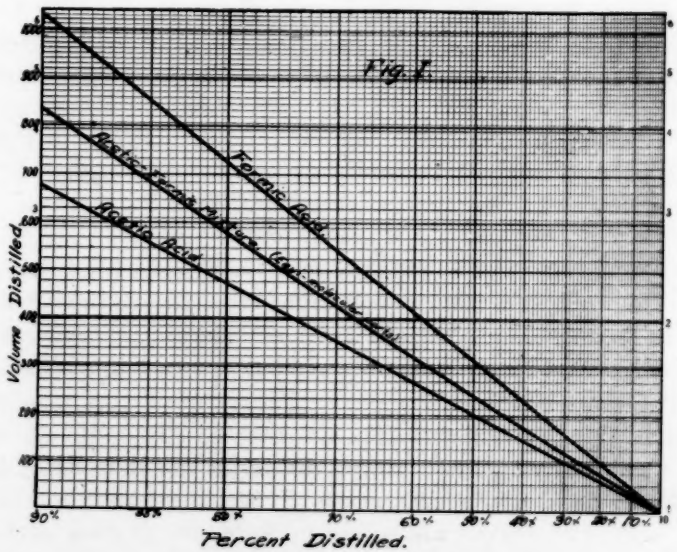

Fig. 1.—Distillation curves for acetic acid, formic acid and an equimolecular mixture of acetic and formic acids.

for computing the total titration, and since the error introduced by using our assumed total value did not materially change the shape of the curve in its lower portion, we preferred to use our method rather than to introduce elaborations which did not bid fair to increase materially the accuracy of our conclusions.

The angle of inclination of the curve is a function of the particular fatty acid present, the slope decreasing as the fatty acids become higher in the series. The rate at which the acid distilled off increases with the higher fatty acids; thus caproic acid distills off completely in 400 c.c., whereas acetic acid requires 2,500 c.c. and formic acid 4,200 c.c. to drive over the last trace of the acid.[1]

The effect of these characteristics on the curve for a mixture of fatty acids is that the curve starts with a gradual slope as the higher fatty acids are driven off, and the slope of the curve increases when the lower fatty acids predominate. Ultimately the curve should parrallel that of the lowest fatty acid present in the mixture, provided the distillation is conducted far enough.

It is evident that the curve for a mixture cannot rise more abruptly than does the curve for the lowest individual fatty acid present. Our results with the stools from breast-fed babies have consistently produced lines rising between the curves for acetic acid and formic acids, proving conclusively that formic acid must be present in the mixture, and in considerable amount. In contrast with this, we found that the curves obtained from stools from babies receiving modified milk formulae had less slope than the acetic acid curve and did not cross it.

The difference between the two types is quite evident from the distillation figures, for the stools from breast-fed babies required a distillation of from 1,300 to 1,700 c.c.; whereas the end point on babies receiving modified milk formulae was reached with a smaller volume of distillate. An example of the titration figures for each class is given in Table 3.

1. METHODS

Suspension of Stool in Distilled Water.—Place a twenty-four hour quantity of feces in a 500 c.c. volumetric flask and add distilled water to fill to the mark and then add 2 c.c. of chloroform. After shaking to disintegrate the larger lumps, allow the flask to stand, with occasional shaking for two hours.

Water Soluble Acidity.—Remove about 75 c.c. of the above suspension and centrifugalize. Pipette 50 c.c. of the clear liquid into an Erlenmeyer flask, add a few drops of phenolphthalein solution and titrate with tenth normal alkali. Express results as cubic centimeters of tenth normal alkali per twenty-four hours of feces.

Volatile Acid.—Shake the suspension of the stool in water and measure off 400 c.c. into a graduated cylinder. Transfer this to a 500 c.c volumetric flask, washing the sides of the cylinder with a little distilled water. Add 0.5 c.c. of phenolphthalein solution and make neutral by the addition, drop by drop, of a 10 per cent. solution of caustic soda. Make up to the 500 c.c. mark with distilled water and transfer to a 1,000 c.c. Erlenmeyer flask. Heat on a water bath under a reflex condensor to bring all soluble matter into solution, shaking

often during the boiling. Cool, add 1 c.c. of chloroform and place in the icebox over night in order to solidify the soaps of the higher fatty acids. Filter through cotton, and then filter through plaited filter, covering the funnel to prevent evaporation, as this filtration may require several hours. Add 20 drops of 85 per cent. phosphoric acid and allow to stand an hour or more in the icebox. Filter through plaited filter, covering the funnel to prevent evaporation.[2]

Transfer 150 c.c. of the final solution, as obtained according to the above directions, to a 500 c.c. round bottom, short, ring neck, pyrex flask; attach to a steam distilling apparatus and mark the level of the liquid in the flask with a black pencil. Bring the steam generator to boiling and the contents of the 500 c.c. flask just to boiling; then allow steam to pass into the flask; light the small burner under the flask, keeping the contents of the flask at constant volume and collect the distillate in 100 c.c. flasks; titrate each 100 c.c., using tenth normal alkali and phenolphthalein. Continue the distillation until the titration value for 100 c.c. of distillate falls to less than 0.2 c.c. tenth normal alkali. Calculate final result by adding all the titration figures and multiplying this by 25/6.

For each run, save and combine all distillates after they have been titrated; concentrate to a volume of about 25 c.c. and use for the identification of the volatile acid or acids present, using the method given by Dyer,[1] or that of Mulliken.[3]

2. CHEMICAL EXAMINATION OF STOOLS

The amounts of water soluble and volatile acid found in the stools examined are shown in Table 2. These figures show that bottle fed infants may eliminate stools which contain much larger amounts of water soluble and volatile acid than is found in the stools from normal breast-fed infants.

Our examination of the stools from breast-fed infants has shown all stools from normal healthy breast-fed infants to have an acid reaction and that the volatile acid present is principally a mixture of acetic and formic acids. Our examination of the stools from bottle-fed infants receiving simple cow's milk modifications has shown that these stools may be acid, neutral or alkaline in reaction, and that the acid stools from such infants contain a volatile acid which we have identified as acetic acid.

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2. In order to expedite filtration we modified our procedure by adding 10 gm. animal charcoal, shaking well, and centrifuging before filtering. In this manner we were able to filter the solution quite rapidly, but were troubled by bumping during distillation due to the precipitation of insoluble calcium phosphate in the flask. For this reason we reverted to the original method, arranging our work so as to allow plenty of time for the filtration.

3. Mulliken: Identification of Pure Organic Compounds, New York, John Wiley & Sons, Ed. 1, 1904, p. 80.

TABLE 2.—Acid Stools from Infants. Water Soluble Acidity and Volatile Acid Content of Stools from Twenty-Four Hours' Amount of Food

Breast-Fed				Bottle-Fed, Cow's Milk, Acid Stools Only			
Number	Water Soluble Acidity, C.c. N/10	Volatile Acid Content, C.c. N/10	Predominating Volatile Acids	Number	Water Soluble Acidity C.c. N/10	Volatile Acid Content, C.c. N/10	Predominating Volatile Acids
33	29.0	11.9	Formic and acetic	1	.....	147.5	Acetic
35	23.0	17.9	Formic and acetic	3	.....	69.0	Acetic
36	22.0	37.0	Formic and acetic	5	.....	46.2	Acetic
43	26.0	95.5	Formic and acetic	6	.....	48.5	Acetic
46	27.5	34.6	Formic and acetic	9	.....	90.0	Acetic
48	52.3	58.1	Formic and acetic	3390	23.0	69.0	Acetic
50	36.9	76.4	Formic and acetic	3507	121.0	151.3	Acetic
62	55.7	66.5	Formic and acetic	3416	35.1	46.2	Acetic
63	22.8	57.8	Formic and acetic	3464	108.9	121.4	Acetic
65	12.1	37.1	Formic and acetic	3484	244.0	147.5	Acetic
66	17.8	79.9	Formic and acetic	3316	16.9	48.5	Acetic
67	23.5	56.8	Formic and acetic	3358	75.6	85.0	Acetic
68	43.6	49.8	Formic and acetic	3337	59.0	60.1	Acetic
69	16.4	31.4	Formic and acetic	3374	10.5	34.7	Acetic
70	40.0	59.5	Formic and acetic	3357	6.0	27.4	Acetic
71	25.0	42.6	Formic and acetic	3495	7.0	19.8	Acetic
72	21.9	42.5	Formic and acetic	3317	6.0	31.5	Acetic
74	20.0	53.8	Formic and acetic	3395	49.0	39.3	Acetic
75	22.5	33.5	Formic and acetic	3407	138.0	149.7	Acetic

TABLE 3.—Titration Values for Distillation of Fatty Acids of Feces from Breast-Fed Babies and Babies Receiving Modified Milk Formulae

Volume Distilled	Breast-Fed Baby 67			Baby Fed on Modified Milk Formulae		
	Titration for Each 100 C.c. Portion	Total Titration	Percentage of Total	Titration for Each 100 C.c. Portion	Total Titration	Percentage of Total
100	3.27	3.27	23.98	11.08	11.08	38.70
200	2.55	5.82	42.60	6.15	17.23	60.18
300	1.90	7.72	56.51	3.72	20.95	73.17
400	1.50	9.22	67.50	2.35	23.30	81.38
500	1.11	10.33	75.63	1.61	24.91	86.98
600	0.85	11.18	81.84	1.11	26.02	90.88
700	0.62	11.80	86.37	0.74	26.76	93.47
800	0.47	12.27	89.82	0.55	27.31	95.37
900	0.36	12.63	92.45	0.39	27.70	96.74
1000	0.28	12.91	94.50	0.33	28.03	97.89
1100	0.24	13.15	96.27	0.24	28.27	98.73
1200	0.19	13.34	97.66	0.23	28.50	99.55
1300	0.19	13.53	99.05	0.13	28.63	100.00
1400	0.13	13.66	100.00			

In our graphic study of the rate of distillation of the volatile acids in the stools we obtained results which are shown by the two typical cases listed in Table 3.

In the case of the breast-fed babies the curves were all found to lie between the curves for pure formic and pure acetic acids. In order to avoid the confusion produced by the plotting of all the curves on one sheet we have made a composite curve which is given as Figure 2. This is nearly a straight line, lying between the formic and acetic acid lines.

In the case of the acid stools from bottle-fed babies the curves were found to lie to the left of the acetic acid curve, indicating a slight amount of higher volatile acid. This is shown in Figure 3.

The marked difference in the nature of the volatile acid present in the two types of stools examined by us has led us to seek for the cause. Our first thoughts turned toward the intestinal bacteriology of the two types of infants under discussion.

BACTERIOLOGY OF INFANTS' STOOLS

The splendid pioneer work of Escherich on the bacteriology of nurslings' stools revealed the fact that the typical flora of these stools was quite different from the flora of the stools of artificially fed infants.

Kendall [4] has summarized this work and that of other investigators very well. He states that culturally, morphologically, and chemically the intestinal flora of breast-fed infants is more homogeneous than that of artificially fed infants.

> In addition to *Bacillus bifidus* and *Bacillus acidophilus*, which compromise a majority of the characteristic intestinal bacteria, small numbers of *Micrococcus ovalis, Bacillus coli, Bacillus lactis aerogenes* and other bacteria are found in the feces of nurslings.
>
> The most distinctive features of the dejecta of artificially fed infants are: the relative increase of gram-negative bacteria of the coli-aerogenes type and of coccal forms of the *Micrococcus ovalis* type, together with a diminution of *Bacillus bifidus*. *B. acidophilus* is relatively more numerous, as a rule, in the artificially fed infant than in the nursling. Proteolytic bacteria of several types are also of frequent occurrence, but they are not commonly found in the dejecta of normal nurslings.

We have made similar observations, finding a predominatingly gram-positive flora in breast milk stools as contrasted with a distinctly gram-negative flora in the dejecta of artificially fed infants.

In the case of nurslings *B. bifidus* is so prominent that from the examination of a direct smear one might consider it to be present in almost pure culture. Closer investigation together with cultural work shows the presence of small numbers of the coli—aerogenes type, *Micrococcus ovalis* and spore bearers.

On the other hand, both direct smears and cultures show that the prominent organisms of the stools of artificially fed infants are those of the coli—aerogenes type (including *B. coli, B. aerogenes, B. acidi*

4. Kendall: Bacteriology, Philadelphia, Lea and Febiger, pp. 584-585.

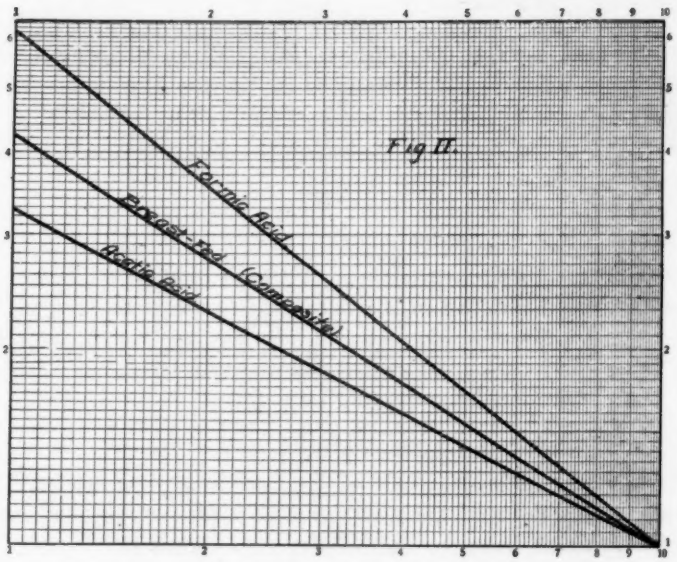

Fig. 2.—Composite distillation curve for breast-fed stools compared with curves for acetic and formic acids.

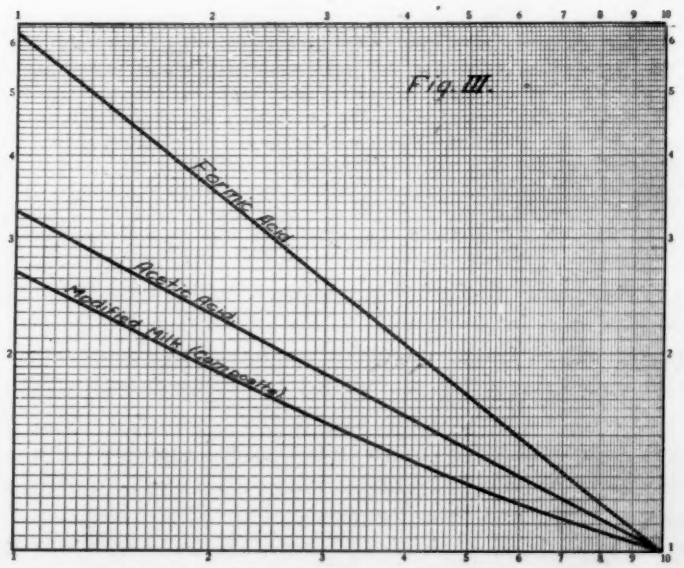

Fig. 3.—Composite distillation curve for modified milk stools compared with curves for acetic and formic acids.

lactici, B. cloacae and *B. capsulatus*) and *Micrococcus ovalis.* Smaller numbers of subtiloid organisms, *B. pyocyaneus* and *B. alkaligenes* were isolated.

Bosworth and Prucha [5] have shown that *B. aerogenes,* one of the most common of the dairy organisms, has the peculiar property of decomposing citric acid, the final end products being water, carbon dioxid and acetic acid. We have found that pure cultures of *B. aerogenes* isolated from the stools of several infants possessed the power of decomposing citric acid in the exact quantitative manner previously shown by Bosworth and Prucha who used cultures of this organism isolated from dairy products.

Our finding that *B. aerogenes* is one of the most common organisms present in the feces from bottle-fed babies, together with the fact that cow's milk, as shown by Bosworth and Van Slyke, contains 0.2 per cent. citric acid, led us to investigate the possible conection which might exist between the presence of citric acid in modified cow's milk and the presence of acetic acid and *B. aerogenes* in the type of stool under discussion.

The question also arose as to whether other fecal organisms might not have this same power of decomposing citric acid with acetic acid as one of the end products. To ascertain this point experiments were undertaken.

Volatile Acids Resulting from the Action of Certain Aerobic Bacteria on Citric Acid.—Fresh specimens were obtained frequently from the babies in the hospital and as many different types of bacteria were isolated and identified as possible.

One hundred c.c. of plain beef extract broth containing 1 per cent. crystallized sodium citrate, with controls of this same broth without the citrate, were inoculated with pure cultures of the different organisms and allowed to grow for several days at 37 C. On distillation with steam after acidifying with sulphuric acid, volatile acid was recovered.

From Table 4 it will be seen that some organisms produced more volatile acid than others, for instance: *B. aerogenes* (No. 6.6), *M. ovalis* (No. 58.4), and an unidentified organism (No. 23.3) produced more than 0.4 gm. of the volatile acid calculated as acetic acid; while *B. capsulatus* (No. 33.4), *B. cloacae* (No. 21.1), *B. coli,* and *B. acidi lactici* (No. 39.4) produced smaller amounts, from 0.15 to 0.22 gm.; and a third class of nonsugar fermenters like *B. subtilis* and *B. alkaligenes* produce practically none, which indicates that the power of producing acetic acid from citric acid is peculiar to only a few organisms.

It will also be noticed that in the controls containing no citrate an appreciable amount of volatile acid was produced, possibly due to the

5. Bosworth and Prucha: J. Biol. Chem. **8**:479, 1910.

breaking down of the peptone contained in the medium. It is apparent that those organisms which produced large amounts of volatile acid from the citrate solution also produced relatively large amounts from the controls, showing that in the absence of citrate in the medium other constituents were attacked.

TABLE 4.—SHOWING DECOMPOSITION OF CITRATE TO ACETIC ACID (?) IN PLAIN BROTH CONTAINING SODIUM CITRATE

Name	Lab. No.	Volatile Acid			Control: No Citric Acid in Media Volatile Acid		
		Days	C.c. N/10 NaOH	Gm. as Acetic Acid	Days	C.c. N/10 NaOH	Gm. as Acetic Acid
B. aerogenes	6.6	4	77	0.462	14	15.4	0.092
		8	78	0.468			
		18	28.6	0.168			
B. aerogenes	51.1	5	65.1	0.390	10	0.0	0.000
		8	60	0.36			
B. aerogenes	53.3	8	20	0.12	17	4.0	0.0024
		11	24.3	0.143			
		14	66.0	0.396			
B. coli	7	11	41.0	0.249			
B. coli	8	4	18.5	0.111			
		9	44	0.264			
		15	10	0.06			
B. acidophilus	2	5	0.0				
		7	5.0	0.03			
		19	25.2	0.15			
B. alkaligenes	15.4	6	0.6	0.0036	8	0.8	0.0048
		8	1.0	0.006			
B. cloacae	21.1	4	37.8	0.226	14	0.5	0.003
		8	44	0.264			
M. ovalis	58.4	4	91.8	0.546	15	13.1	0.078
			87.5	0.52			
B. capsulatus	33.4	5	25	0.15	15	13.1	0.18
		14	31.8	0.18			
B. acid lactici	39.4	5	25	0.15			
		14	9.3	0.055			
Subtiloid organism	45.5	5	0.0	.....	11	1.5	0.009
		11	2.2	0.013			
B. morgans I	24.4	5	30.0	0.18	12	2.8	0.0168
		8	27.2	0.143			
Coccus	59.4	6	4.0	0.024	12	2.1	0.012
		8	1.4	0.084			
		12	5.6	0.033			
Unidentified	23.3	5	72.5	0.435	16	6.0	0.036
		11	66.5	0.399			
		14	74.6	0.447			
Unidentified	34.4	5	5.0	0.03	16	0.5	0.003
		12	17.9	0.105			
Unidentified	36.3	6	37.1	0.222	8	2.2	0.013
		8	22.2	0.133			

In an effort to obtain quantitative data the medium used by Bosworth and Prucha [5] was tried. This medium was made according to the following formula:

MEDIUM 1: Acid sodium phosphate, 5 gm.; magnesium sulphate, 5 gm.; potassium chlorid, 0.5 gm.; official ammonium citrate solution [5] 50 c.c.; water to make 1,000 c.c.

B. aerogenes and Organism 23.3 grew luxuriantly in this medium within twenty-four hours, but other organisms grew only faintly or not at all.

Portions of this medium were inoculated with pure cultures of those organisms which thrived in it and after three or four days were

tested for citric acid. As soon as all the citrate had disappeared, 100 c.c. were distilled with steam after acidifying with sulphuric acid and the volatile acid recovered and identified by the formation of acet-p-toluide.

The results are tabulated in Table 5 and they show that while all the organisms tested destroyed the citric acid, only two of them, *B. aerogenes* and the unidentified Organism 23.3, produced acetic acid.

TABLE 5.—SHOWING DECOMPOSITION OF CITRIC TO ACETIC ACID IN MEDIUM 1

Name	Lab. No.	Time Citric Acid Disappeared, Days	Volatile Acid		Melting Point of Toluide
			C.c. N/10 NaOH	Gm. as Acetic Acid	
B. aerogenes	4	5	88.5	0.531	147
B. aerogenes	6.6	4	80.0	0.48	147
B. aerogenes	42.3	8	79.0	0.479	147
B. aerogenes	20.6	3	87.0	0.52	147
B. aerogenes	13.1	7	70.0	0.42	146
B. aerogenes	38.4	5	70.0	0.42	146
B. aerogenes	20.7	4	11.5	0.429	147
Unidentified	23.3	4	70.0	0.42	147
Coccus	44.3	12	0.0	0.00	
Unidentified	58.3	13	0.4	0.0024	
Unidentified	34.4	11	0.5	0.003	

As the Bosworth and Prucha medium proved unsatisfactory for the growth of all but a few organisms, it was modified by the addition of 0.3 per cent. beef extract.

MEDIUM 2: Acid sodium phosplate, 5 gm.; magnesium sulphate, 5 gm.; potassium chlorid, 0.5 gm.; official ammonium citrate solution [5] 50 c.c.; Liebig's beef extract, 3 gm.; water to make 1,000 c.c.

This medium was inoculated with pure cultures and good growths were obtained. The growths were tested for volatile acid and the results are given in Table 6.

Only one organism (No. 58.4), which is probably *M. ovalis,* produced acetic acid. The others, including *B. cloacae, B. coli, B. capsulatus, B. acidi lactici* and several unidentified organisms, required more or less time, ranging from three to fourteen days, to dispose of the citrate but produced no acetic acid.

Study of the Source of Formic Acid.—In order to determine the source of formic acid which we found to be present in the stools from breast-fed babies we referred to the study of the bacterial flora of the feces of breast-fed babies which has been conducted by Brown and Bosworth.[6] As such feces show a characteristic predominance of *B. bifidus,* we conducted an investigation of the metabolism of *B. bifidus* in the presence of citric acid in order to determine if this organism in the process of decomposing citric acid produces formic acid.

After several unsuccessful attempts, growth was produced in a neutral beef extract broth medium containing ½ per cent. sodium

6. Brown, E. W., and Bosworth, A. W.: Am. J. Dis. Child. **23**:243 (March) 1922.

citrate. One specimen produced sufficient volatile acid to give a good curve (Fig. 4).

The curve of the fatty acids from *B. bifidus* is neither a formic acid curve nor an acetic acid curve nor does it coincide with the composite curve for fatty acids from the stools of breast-fed babies. It lies to the left of the composite, therefore indicating a greater percentage of acetic acid than does the average stool from breast-fed babies. It appears that there may be present in the intestines some other organism which can produce a higher percentage of formic acid than does *B. bifidus,* or else the percentage of formic acid produced varies with changing conditions in the intestinal tract. It is to be regretted that circumstances prevent the authors from definitely

TABLE 6.—SHOWING DECOMPOSITION OF CITRIC TO ACETIC ACID IN MEDIUM 2

Name	Culture No.	Time Citric Acid Disappeared, Days	Volatile Acid		Melting Point of Toluide
			C.c. N/10 NaOH	Gm. as Acetic Acid	
M. ovalis	58.4	10	59.0	0.354	147
B. coli	7	10	0.4	0.0024	
B. coli	26.1	14	1.2	0.0072	
B. coli	60.1	4	0.35	0.0021	
B. coli	58.2	8	20.0	0.12	
B. morgans I	24.4	18	0.7	0.0042	
B. morgans I	39.7	21	0.4	0.0024	
B. morgans I	21.5	14	4.7	0.0282	
B. cloacae	21.1	4	1.0	0.006	
B. cloacae	20.1	3	0.1	0.0006	
B. capsulatus	33.4	4	0.4	0.0024	
B. capsulatus	17.6	3	0.5	0.0003	
B. acidi lactici	4.3	4	0.7	0.0042	
B. acidi lactici	14.1	18	0.5	0.0030	
Dysentery-like	34.1	4	0.2	0.0012	
B. acidophilus	2	4	0.7	0.0042	
Coccus	44.3	3	0.3	0.0018	
	stock cult.				
B. proteus	27				
B. proteus vulgaris	28				
Unidentified	34.4	4	0.3	0.0018	
Unidentified	36.3	4	0.35	0.0021	
Unidentified	23.1	3	0.6	0.0036	
Unidentified	23.4	3	0.2	0.0012	

answering, for the present, this most interesting and important question. It must suffice for the present to offer the suggestion that our observations indicate that *B. bifidus* may attack citric acid with the production of two acetic acid molecules and one formic acid molecule for each molecule of citric acid.

Can the Acetic Acid Content of Infants' Stools Be Increased by the Addition of Citrate to the Food?—Our finding that certain organisms, present in the stools from bottle-fed infants, possess the property of producing acetic acid from citric acid has led us to investigate the possibility of increasing the acetic acid content of stools by the addition of citrate to the food. This was done in the manner indicated in Table 7.

In connection with the data given in Table 5 it is of interest to note the following facts: When a synthetic food containing no citrate is fed to an infant, no acetic acid appears in the stools; when the same food containing a soluble citrate (sodium citrate) is fed, a small amount of acetic acid appears in the stools; and when the same food containing an insoluble citrate (calcium citrate) is fed a large amount of acetic acid appears in the stools.

The addition of soluble citrates (sodium citrate or orange juice) to modified milk formulas increases only slightly the acetic acid contents of the stools, while the addition of an insoluble citrate (calcium citrate) to the same formulas results in a marked increase in the acetic acid contents of the stools.

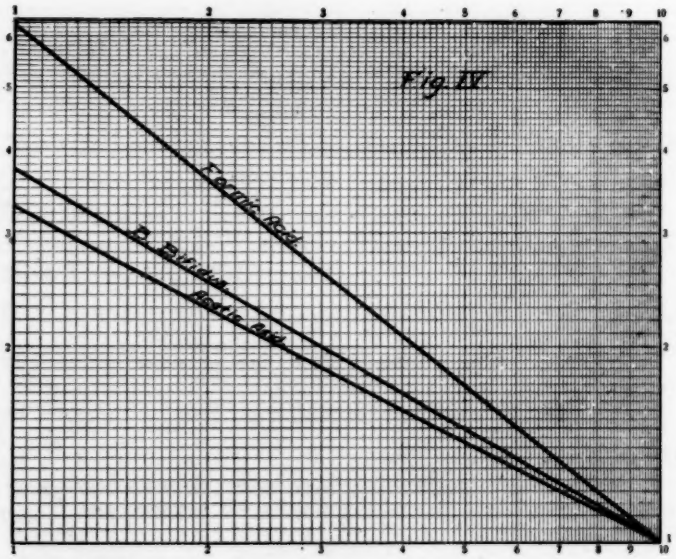

Fig. 4.—Distillation curve from culture of *B. bifidus* compared with curves for acetic and formic acids.

The stools from infants receiving Dryco dry milk contain large amounts of acetic acid. This is probably due to the fact that a considerable portion of the soluble citrate, originally present in the milk, is converted to insoluble calcium citrate during the process of drying.

The explanation offered for the observations contained in this paper are as follows: While cow's milk, like human milk, contains about 0.2 per cent. citric acid, present in the form of soluble citrates, cow's milk, unlike human milk, contains a considerable quantity of soluble calcium salts in its whey or serum. Milk, on entering the intestines, encounters an alkaline or neutral condition and this condition induces a chemical rearrangement among the milk constituents which results, in

the case of cow's milk, in the precipitation of insoluble calcium citrate. As this insoluble calcium citrate cannot be absorbed by the intestines, it becomes part of the waste matter which moves along the whole intestinal tract. Here it is subjected to attack by the bacteria present with the results noted in this paper.

There may be come clinical significance to the presence of the insoluble citrate in the intestines if we remember that citrates, as shown by Bosworth and Prucha, may take the place of sugar for certain organisms and, therefore, acting as a protein sparer, prevent or retard putrification within the intestines, an important point to be considered in view of the recent work of one of us,[7] which shows

TABLE 7.—SHOWING RELATION OF ACETIC ACID IN STOOLS TO CITRATE IN FOOD

Case No.	Kind of Food	Formula F–S–P	Volume of Food per 24 Hrs., C.c.	Amount of Citric Acid in Milk per 24 Hrs., Gm.	Amount and Kind of Citrate Added per 24 Hours	Acetic Acid in Stools, Gm. per 24 Hours	Reaction of Stools Toward Litmus Paper
475	"Synthetic milk"	2–5–1.6	1,440	None	None	None*	Alkaline and neutral
475	"Synthetic milk"	3–6–1.6	1,440	None	2.88 gm. of sodium citrate	0.370	Acid and neutral
475	"Synthetic milk"	3–6–1.6	1,440	None	1.5 gm. of calcium citrate	0.642	Acid
475	Modified milk	2–6–1.6	1,440	1.44	None	0 855	Acid
475	Modified milk	2–6–1.6	1,440	1.44	1.5 gm. of calcium citrate	1.213	Strongly acid
479	Modified milk	2–5–1.6	1,440	1.44	None	0.278	Acid
479	Modified milk	2–5–1.6	1,440	1.44	2 gm. of sodium citrate	0.372	Acid
479	Modified milk	2–5–1.6	1,440	1.44	2 gm. of calcium citrate	0.840	Strongly acid
489	Modified milk	2.5–6.5–2	1,080	1.34	None	0.540	Acid
489	Modified milk	2.5–6.5–2	1,080	1.34	Orange juice	0.640	Acid
493	Dryco dry milk	1.2–4.4–3.4	1,000	2.13	None	0.907	Alkaline

* Contained a small amount of volatile acid which was not acetic acid.

that the feces from bottle-fed infants contain more nitrogenous matter than is the case with breast-fed infants.

Another point to be considered also is what detrimental effect the loss of the citrate may produce. Citric acid is a normal constituent of both human milk and cow's milk. Its presence in milk may be taken as an indication that it serves some purpose in the animal metabolism. Citric acid is not only an acid but it is also an alcohol as may be seen from its structure.

As an alcohol it may form esters and in this connection the destructive action of heat upon the antiscorbutic vitamin in milk would suggest the possibility that this vitamin may be an ester-like compound of some of the citric acid in milk.

7. Bosworth, A. W.: Am. J. Dis. Child. **22**:613 (Dec.) 1921.

SUMMARY

1. A method is given for the distillation of volatile acids from infants' stools.

2. A graphic method is given for the study of the nature of the volatile acids which may be distilled from infants' stools.

3. The stools from normal healthy breast-fed infants have been found to be acid in reaction and to contain the volatile acids, formic and acetic.

4. The stools from healthy bottle-fed infants have been found to be acid, neutral or alkaline in reaction. The acid stools may contain very large amounts of acid and the volatile acid present is acetic acid

5. *B. aerogenes, M. ovalis, B. bifidus,* and other unidentified organisms isolated from acid stools of babies possess the power of reducing citrate to a volatile acid.

6. The volatile acid produced by *B. aerogenes, M. ovalis,* and other unidentified organisms was determined to be acetic acid.

7. The volatile acid produced by *B. bifidus* was determined to be a mixture of acetic and formic acids.

8. Other organisms like *B. coli, B. capsulatus, B. acidi lactici,* and *B. cloacae* disposed of the citrate producing carbon-dioxid and water without the formation of acetic acid.

9. If a synthetic food containing no citrate is fed to an infant, no acetic acid appears in the stools.

10. If a synthetic food containing a soluble citrate (sodium citrate) is fed to an infant, a small amount of acetic acid appears in the stools.

11. If a synthetic food containing an insoluble citrate (calcium citrate) is fed to an infant a large amount of acetic acid appears in the stools.

12. The addition of soluble citrates (sodium citrate or orange juice) to modified milk formula increases only slightly the acetic acid contents of the stools.

13. The addition of an insoluble citrate (calcium citrate) to modified milk formulas results in a marked increase in the acetic acid content of the stools.

14. The stools from infants receiving Dryco dry milk contain large amounts of acetic acid. This is probably due to the fact that a considerable portion of the soluble citrate, originally present in the milk, is converted to insoluble calcium citrate during the process of drying.

PROGRESS IN PEDIATRICS

REVIEW OF THE LITERATURE ON RESPIRATORY DISEASES FROM JANUARY, 1920, TO JUNE, 1921 *

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(Concluded from page 282)

PNEUMONIA

Pathogenesis.—The studies on experimental pneumonia of Cecil and Blake [63] comprise an unusually important series of articles. These articles deserve a very careful reading as does also a single article by Cecil [64] which gives a short and excellent exposition of the bacteriology and mode of infection of pneumonia. These investigators concluded that while the pneumococcus is the specific cause of lobar pneumonia, it is unable to initiate an infection of the normal mucous membranes of the upper respiratory tract, or to produce pneumonia following intravenous injection, but it must gain access to the lower respiratory tract by way of the trachea in order to cause pneumonia. Lobar pneumonia is therefore bronchiogenic in origin, the invasion of the blood-stream by pneumococci in this disease being secondary to the invasion of the lungs. The pneumococcus primarily invades the lung tissue at some point or points near the root of the lobe, and thence spreads throughout the lobe by way of the perivascular, peribronchial and septal tissues, and the lymphatic system. The alveolar structure

* Received for publication Dec. 22, 1921.

* From the Department of Pediatrics of Cornell University Medical College.

* This review was originally undertaken by Dr. Louis C. Schroeder, but after reviewing more than fifty articles, he was forced by pressure of other work to relinquish this study. He very generously contributed his notes to me for which I make grateful acknowledgment.

63. Cecil, R. L., and Blake, F. G.: Studies on Experimental Pneumonia: I. Production of Pneumococcus Lobar Pneumonia in Monkeys, J. Exper. M. **31**: 403 (April) 1920. II. Pathology and Pathogenesis of Pneumococcus Lobar Pneumonia in Monkeys, Id. **31**:445 (April) 1920. III. Spontaneous Pneumonia in Monkeys, Id. **31**:499 (May) 1920. IV. Results of Prophylactic Vaccination against Pneumococcus Pneumonia in Monkeys, Id. **31**:519 (May) 1920. V. Active Immunity against Experimental Pneumococcus Pneumonia in Monkeys Following Vaccination with Living Cultures of Pneumococcus, Id. **31**:657 (June) 1920. VI. Active Immunity Following Experimental Pneumococcus Pneumonia in Monkeys, Id. **31**:685 (June) 1920. VII. Treatment of Experimental Pneumococcus Type I Pneumonia in Monkeys with Antipneumococcic Serum, Id. **32**:1 (July) 1920. VIII. Experimental Streptococcus Hemolyticus Pneumonia in Monkeys, Id. **32**:401 (Oct.) 1920.

64. Cecil, R. L.: Bacteriology and Pathogenesis of Pneumonia, New York M. J. **113**:728 (May 18) 1921.

becomes primarily infected by spread of the pneumococci from the grosser framework of the lungs into the alveolar walls, and thence into the alveolar spaces with the exudate. Hepatization usually occurs first in the posterior and upper parts of the lower lobes, in the lower part of the middle lobe, and in the lower and posterior parts of the upper lobe.

Cecil and Blake further stated that the mode of infection in *Streptococcus hemolyticus* pneumonias is similar to that in the penumococcus pneumonias, as above, but while the influenza bacillus enters by passing down the bronchial tree, it lacks the invasive character of the other two microorganisms. Hence, the lesions produced by this bacillus are focal while those produced by the pneumococcus and the streptococcus involve extensive areas.

Cecil urged discarding the terms "bronchopneumonia" and "lobar pneumonia" for *Streptococcus hemolyticus* or *S. viridans* pneumonia, pneumococcus pneumonia, influenza bacillus pneumonia, etc.

Wherry and Butterfield [65] were not able to produce pneumonia in mice after spraying with virulent pneumococci. Their experiments showed that the type M 5 of the *Bacillus enteritidis* is inhaled by mice into the deepest alveoli or capillary bronchi of the lungs, and that primary pneumonia follows in the case of this microorganism, which is capable of growing and producing its toxins there, whereas the virulent pneumococci gradually disappear.

Foster [66] stated that any circumstance which lowers the vitality of the human organism as a whole, or by irritation injures the pulmonary tissues locally, predisposes to a primary bronchopneumonia. The invader is always at hand and the invasion depends on the host. He called attention to the fact that primary bronchopneumonia is not limited to childhood and old age but is a common affection in young robust adults, though easily overlooked.

Bacteriology of Pneumococcus Pneumonias.—Spooner [67] tabulated the statistics found by eleven authors as to the relative frequency of occurrence of the various types of the pneumococci in lobar pneumonia. Of a total of 2,980 cases, 29 per cent. were Type I; 21 per cent. were Type II; 11 per cent. were Type III, and 39 per cent. were Type IV. He urged the careful use of Type I serum in the treatment of Type I cases.

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65. Wherry, W. B., and Butterfield, C. T.: Inhalation Experiments on Influenza and Pneumonia, and on the Importance of Sprayborne Bacteria in Respiratory Infections, J. Infect. Dis. **27**:315 (Oct.) 1920.

66. Foster, N. B.: Notes on the Diagnosis of Bronchopneumonia and Its Complications, Am. J. M. Sc. **161**:1 (Jan.) 1921.

67. Spooner, L. H.: The Specific Diagnosis and Treatment of Acute Lobar Pneumonia, Boston M. & S. J. **182**:389 (April 15) 1920.

Locke, Thomas, and O'Hara [68] reported that they had on their pneumonia service at the Boston City Hospital, ninety-four cases of lobar pneumonia in children under 15 years of age of which only four died. Forty-two cases were typed, and revealed that of these, eleven were Type I; five were Type II; four were Type III, and twenty-two were Type IV. Of the four fatal cases, two were untyped, one was Type I and one was Type IV. Because of the low mortality, no antipneumococcus treatment was given to those patients who were under 5 years of age.

Armstrong [69] in England reported rather contradictory findings to those of the Boston investigators. He noted that the Type I pneumococcus, though responsible for many cases of lobar pneumonia in adults, does not appear to cause the disease in childhood. In only one case was a Type I pneumococcus isolated from a child. The pneumococci he found most responsible for the disease in young children belonged almost uniformly to Type II. Type III seemed in the upper respiratory tract to have only a limited distribution.

For rapid pneumococcus typing, Oliver [70] described a precipitin test of filtered pneumonic sputum to which bile has been added. By this method the typing may be effected within half an hour after the receipt of the sputum.

According to Nobécourt, Paraf and Bonnet,[71] at the Paris Maternité, during 1919, all the infants and adults were systematically examined for pneumococci with 55 per cent. positive results from 322 smears. Type III was found in 133 cases and was responsible for most of the infections. When a carrier of Type II had been admitted to the ward, this type appeared almost at once in the other women and infants and a train of infectious processes in the upper air passages followed. They considered it especially important to guard infants against this infection. The infant should be taken away from its mother if the latter becomes affected and be brought to her only to be nursed, and the mother should wear a veil while nursing.

Sailer, Hall, Wilson and McCoy,[72] reported a study of pneumococcus carriers. They believe strongly that active methods of disinfection should be carried out against pneumococcus carriers and that

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68. Locke, E. A.; Thomas, H. M. Jr., and O'Hara, D.: Acute Respiratory Infections at the Boston City Hospital, Boston M. & S. J. **183**:480 (Oct. 21) 1920.

69. Armstrong, R. R.: The Serologic Characters of Disease-Producing Pneumococci, Brit. M. J. **1**:259 (Feb. 19) 1921.

70. Oliver, W. W.: A Rapid Method of Pneumococcus Typing, J. Infect. Dis. **27**:310 (Oct.) 1920.

71. Nobécourt, P.; Paraf, J., and Bonnet, H.: Pneumococcus Infection in Infants, Presse Méd. **28**:313 (May) 1920. Abstr. J. A. M. A. **75**:137, July 10) 1920.

72. Sailer, J.; Hall, M. W.; Wilson, R. L., and McCoy, C.: A Study of Pneumococcus Carriers, Arch. Int. Med. **24**:600 (Dec. 15) 1919.

all contacts of cases of pneumonia should be cultured as are meningitis contacts. They described the results of numerous means of disinfection, the most valuable of which proving to be oily solutions of phenol and iodin.

Thomas and Parker [73] studied the bacteriology of lobar pneumonia by means of lung punctures. They found, according to Locke, Thomas and O'Hara,[68] a mortality of 56 per cent. in cases in which viable organisms were obtained by lung puncture after the fifth day of the disease, whereas cases which yielded no organisms by lung puncture irrespective of the day of the disease, recovered with only two exceptions, or 6.5 per cent. They found that destruction of the organisms is the first step in the process of recovery, but also that crisis may occur before the organisms have been entirely killed, or not until several days after. This led them to the belief that the antibacterial forces may proceed at one rate of speed while the detoxifying mechanism is going on at a different rate, and they concluded that the death of the pneumococcus is not the factor which causes or initiates crisis.

Pathology.—Berry [74] made a careful analysis of the necropsy findings in 400 fatal cases of lobar pneumonia, and noted a number of outstanding features, of which several are already well recognized. He noted, however, that the pericardium is affected in varying degree in almost one third of the cases, but that true acute nephritis as a complication or sequel of lobar pneumonia is unusual, if not rare. He found that the products formed or eliminated by, or as a result of the pneumococcus and occasional other organisms in lobar pneumonia, produce a general toxemia with definite reactions and lesions in many organs of the body. Grossly, these changes are best and most frequently seen in the spleen, kidneys, liver and heart, whereas histologically they are found still more commonly in the suprarenals and pancreas. Acute sinusitis and otitis media are decidedly uncommon in lobar pneumonia in adults, which fact he feels would strengthen the idea suggested by Blake and Cecil, that the pneumococcus by itself is of relatively low pathogenicity for the upper respiratory tract.

Meakins [75] studied a number of cases of pneumonia to determine the quantity and quality of the expired air and found that as the respiration increased, there was a gradual decrease in the volume per respiration though the total ventilation per minute showed a conspicuous increase.

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73. Thomas, H. M., Jr., and Parker, F. Jr.: Results of Antimortem Lung Punctures in Lobar Pneumonia: Their Bearing on the Mechanism of Crisis, Arch. Int. Med. **26**:125 (July) 1920.

74. Berry, F. B.: Lobar Pneumonia: An Analysis of 400 Autopsies, M. Clinics N. America **4**:571 (Sept.) 1920.

75. Meakins, J.: Harmful Effects of Shallow Breathing with Special Reference to Pneumonia, Arch. Int. Med. **25**:1 (Jan.) 1920.

He concluded that the point might be reached where the alveolar air inspired or expired might amount to a comparatively few cubic centimeters, being undoubtedly insufficient to carry on adequate pulmonary ventilation so that eventually anoxemia and cyanosis would develop. He further noticed in his cases that with increased respiration, the oxygen content of the expired air became higher and the carbon dioxid content lower so that a respiratory quotient above one occurred. But with crisis there was a rapid return to normal not only of respiratory quotient but also of respiratory rate, respiratory volume and total ventilation per minute. He thought it not probable that this is due to any conspicuous change in the damaged lung. He concluded, therefore, that the anoxemia and cyanosis occurring in lobar pneumonia is the result of the rapid and shallow breathing typical of the condition, and he also noted the well recognized harmful effect of persistent anoxemia on the cardiovascular system.

Methemoglobin in pneumonia was studied by Stadie [76] who noted that in the occasional cases of this disease which show a decrease in the oxygen capacity of the blood, the decrease is probably due to a formation of methemoglobin. The latter is removed from the circulation, however, as rapidly as it is formed, so that it can seldom be detected even qualitatively, and is probably never a cause of cyanosis.

A study of water retention in pneumonia was made by Lussky and Friedstein [77] who called attention to the fact that coincident with defervescence in febrile diseases there is a loss of weight, and that this loss is especially likely to occur in pneumonia. They were unable to find any relationship between the rapidity of the loss and either the degree or the duration of the fever. The absorption and excretion of the inflammatory exudate or of its products, as shown by an increased amount of urine as well as by the excreted amounts of chlorids and nitrogen, cannot explain the whole story. They are of the belief that the loss of weight coincident with or slightly preceding the abrupt fall in temperature is best explained by the theory that water which is usually at the disposal of the organism for purposes of heat regulation becomes not available for this purpose, being possibly bound within the organism in such a way that it cannot exercise its heat dissipating function by evaporation from the body surfaces and lungs. With restoration of the water binding power of the tissues to the normal, which may occur more or less abruptly, water would be liberated for heat regulatory purposes and elimination in the urine.

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76. Stadie, W. C.: Studies in Blood Changes in Pneumococcus Infection. An Experimental Study of the Formation and Fate of Methemoglobin in the Blood, J. Exper. M. **33**:627 (May) 1921.

77. Lussky, H. O., and Friedstein, H.: Water Retention in Pneumonia, Am. J. Dis. Child. **19**:337 (May) 1920.

In this way, the loss of weight coincident or shortly preceding the abrupt fall of temperature could be explained.

Symptomatology, Diagnosis and Occurrence.—Abrahams [78] made a clinical summary of 558 cases of untyped lobar pneumonia seen among the soldiers of the British Army command at Aldershot during 2½ years of the war period. The initial symptoms or complaints he tabulated as follows:

Shivering, 69 per cent.; pain in side, 60 per cent.; headache, 35.6 per cent.; vomiting, 33 per cent.; cough, 24 per cent.; pains all over, 9 per cent.; general malaise, 7.6 per cent.; bronchitis, 7 per cent.; pain in abdomen,[79] 5.5 per cent.; tonsillitis, 2.3 per cent.; dyspnea, 2 per cent.; hemoptysis, 1.6 per cent.; diarrhea and vomiting, 0.5 per cent.

Wilcox [80] called renewed attention in his study of the symptomatology of childhood to the fact that the physical signs of the chest are affected by certain structural differences peculiar to youth, such as the thin elastic chest wall, and the relatively larger space occupied by the bronchial tree. In particular, the intensified breath sounds, normally heard at the right apex anteriorly in the adult, are so much more marked in children as to make this a difficult area in which to interpret uncertain physical signs. Doubt as to the existence of a lesion at the right apex often may be cleared up by comparison of the physical signs here and in the axilla, as in the latter location physiologic conditions affecting the signs anteriorly do not obtain, while a pathological lesion of the apex of the lung should produce much the same symptoms in the axilla as anteriorly or posteriorly. He cited the case of an infant in whom the physical signs over the right apex anteriorly of distinctly impaired resonance and high pitched breath sounds with a slightly bronchovesicular element, together with a head cold, fever and increased respiratory rate, seemed all to justify the diagnosis of pneumonia in the right upper lobe. However, the physical signs were normal in the apex of the right axilla, and incision of a bulging right ear drum terminated all symptoms.

Freeman [81] reproduced roentgenograms showing apparently peripheral pneumonic consolidation in three children in whom repeated examination failed to reveal any physical signs of pneumonia, not even

78. Abrahams, A.: Lobar Pneumonia: A Clinical Analysis of 558 Consecutive Cases, Lancet **2**:543 (Sept. 11) 1920.

79. Of the thirty-one patients in whom the initial complaint was pain in the abdomen, seven were admitted as cases of appendicitis, six were sent to the operating room, and three were actually operated on, but normal appendices were found.

80. Wilcox, H. B.: Some peculiarities in the Symptomatology of Childhood, Arch. Pediat. **37**:577 (Oct.) 1920.

81. Freeman, R. G.: Pneumonia in Infancy and Childhood without Physical Signs, Arch. Pediat. **37**:11 (Jan.) 1920.

a markedly increased rate of respiration. In all three cases, approximately the same portion of the right upper lobe was involved, and Freeman thought that the signs were obscured because to hear them one would have to do so through the right scapula. He thought it remarkable that these children gave no signs of consolidation in the axilla.

Blauner [82] considered the diagnosis of pneumonia in infancy and early childhood to be based distinctly on physical signs since its symptoms in children, especially the fever, may be very variable. He believed that central lobar pneumonia does not exist, and that when this pneumonia does exist, it can be found by delicate percussion though bronchial breathing will only be present if the wedge-shaped area of consolidation extending in from the cortex reaches the hilum or is in communication with a bronchus. Bronchopneumonia, however, may give no physical signs other than those of a bronchitis. In children the physical signs of resolution may be those of a quick liquefaction of the consolidation with rales redux, or the resolution may be slow, lasting from three to seven days, the physical signs melting into normal signs. Râles play a very unimportant rôle in children, and may be absent throughout a pneumonia.

Gunewardene [83] reported a case of central pneumonia in a child of 2 years in which the physical signs of consolidation did not appear until the ninth day, and crisis did not occur until the fourteenth day.

In a report of 200 necropsies on infants who were still-born or who died within the first week of life, Warwick [45] described four cases of bronchopneumonia of which one was that of a full term infant who lived only 2½ hours, and presented at necropsy a very typical bronchopneumonia. Smears from the lung showed polymorphonuclear leukocytes and gram-positive cocci in pairs and chains. Warwick felt that there was but little doubt that this condition developed in utero although the mother appeared to be entirely normal.

Nobécourt [84] discussed the cases of two children of 7 and 15 years in whom the symptoms at the onset were delirium and extreme excitement which in the older girl were preceded by a stage of torpor suggesting coma. Meningitis was suggested, but the spinal fluids were practically normal. The signs of pneumonia appeared, clearing up the diagnosis, and both patients recovered. He noted that these brain disturbances may take the form of convulsions, delirium or most

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82. Blauner, S. A.: Physical Signs of Pneumonia in Children, New York M. J. **112**:1032 (Dec. 25) 1920.

83. Gunewardene, H. O.: Central Pneumonia in a Child of Two, Lancet **2**: 73 (July 10) 1920.

84. Nobécourt, P.: The Brain and Meninges in Pneumonia in Children, Bull. méd., Par. **35**:209 (March 12) 1921. Abstr. J. A. M. A. **76**:1281 (April 30) 1921.

frequently somnolence which may come with the rise of temperature. Extreme general hyperaesthesia and ocular disturbances are frequent. The outlook is somewhat serious even with a serous meningitis, and of course grave with purulency. He stated that the treatment must be prompt and vigorous, being to relieve congestion of the nerve centers as by hot baths or packs every four to six hours. Lumbar puncture should be done once anyway if it is a serous meningitis, repeatedly, if a purulent meningitis.

Sequels and Complications.—Overend [85] made a plea for the more frequent radiologic examination of the chest in children, particularly in those who fail to recover completely after pneumococcal infections of the lungs. He stated that many cases of ill health in children after pneumonia and other infectious diseases are due to unresolved pneumonia produced by a chronic pneumococcal infection and are not tuberculous. Bronchiectasis is likely to follow attacks of chronic or indurative basal pneumonia; disseminated patches of broncho-pneumonia are more liable to produce areas of diffuse bronchial dilatation.

Packard [86] drew attention to the fact that because of the recent high incidence of pneumonia, a great many chronic lung changes will be encountered in the next few years. He felt that with due allowance for the normal variations in children, abnormal physical signs at one apex should be considered as due to pulmonary tuberculosis until proved not to be, while those at the base should be looked on as non-tuberculous until definitely proved otherwise.

In a paper on chronic nontuberculous lung infection, Field [87] reviewed the literature on this condition and emphasized its diagnostic features. Cases with chronic cough which is not paroxysmal, purulent sputum which is persistently negative for acid-fast bacilli, insignificant radiologic findings with râles located in the lower half of the chest (in the absence of a heart lesion), and the general health only slightly impaired, these, he said, are undoubtedly cases of chronic nontuberculous lung infection.

Radin [88] described twelve cases of chronic lung disease following the influenza epidemic, in all of which the pathologic process was at the base of the lungs, except in three cases which proved to be tuberculous. Sputum was absent in the pleuritis cases as a general rule but was copious in the bronchitis cases. Improvement was the rule, but slow.

85. Overend, W.: Basal Pneumonic Residues in Children, Tubercle **1**:547 (Sept.) 1920.

86. Packard, E. N.: Nontuberculous Lung Changes Following Pneumonia, J. A. M. A. **75**:1537 (Dec. 4) 1920.

87. Field, C. G.: Chronic Nontuberculous Lung Infection, Am. J. M. Sc. **159**:442 (March) 1920.

88. Radin, M. J.: Chronic Lung Disease Following the Influenza Pandemic of 1918-1919, Am. J. M. Sc. **160**:233 (Aug.) 1920.

Several apparently unusual complications have been reported. Fleischner's [89] patient apparently inhaled some sand, and developed a bronchopneumonia. On the eighth day, his heart was noted as markedly displaced to the right, the cause not being made out until six days later when an extensive subcutaneous emphysema appeared beginning in the right supraclavicular space. It was thought that the cardiac displacement was due to an extensive mediastinal emphysema since at no time could a pneumothorax be detected. Thomas and O'Hara [90] reported a case of pneumococcus Type I vegetative endocarditis following lobar pneumonia, and felt that there is some cause for believing that the Type I organism is mainly responsible for pneumococcus endocarditis.

Kerr [91] considered that acute gastric dilatation is a positive danger to the child's life in one out of every four cases of lobar pneumonia. The first symptoms of this complication are usually those of restlessness accompanied by an increased thirst and vomiting. Acute epigastric pain may or may not be in evidence. The respirations are either increased or the breathing much more embarrassed, and there is every evidence of increased exhaustion including cyanosis. These symptoms, however, are inconstant. Examination often reveals a visible and palpable tumor in the upper abdomen. Usually after the first few hours, the pinched features and the objective evidences of circulatory shock are marked. The treatment of this condition must be prompt. If the fluid content of the stomach is marked, Kerr said to place the patient on the left side of the chest anteriorly, and raise the foot of the bed; then perform an efficient lavage; and then withhold everything by mouth at least twelve hours.

In a discussion of the abdominal reflexes in pneumonia, Pastore [92] referred not to those cases wherein the abdominal symptoms usher in pneumonia in children, and subside as the pneumonia becomes installed, but to those in which appendicitis is simulated as a complication of pneumonia, or actually exists as such a complication. The practitioner must keep his eye on the lung in appendicitis and on the appendix in pneumonia.

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89. Fleischner, E. C.: Heart Displacement Apparently Due to Mediastinal Emphysema Following Aspiration Pneumonia, Am. J. Dis. Child. **21**:206 (Feb.) 1921.

90. Thomas, H. M., Jr., and O'Hara, D.: Pneumococcus Type I Vegetative Endocarditis: Report of a Case Following Lobar Pneumonia, Johns Hopkins Hosp. Bull. **31**:417 (Nov.) 1920.

91. Kerr, LeG.: The Mortality Factors of Lobar Pneumonia in Children, New York State J. M. **20**:348 (Nov.) 1920.

92. Pastore, S.: Abdominal Reflexes with Pneumonia, Policlinico **27**:1406 (Dec. 6) 1920. Abstr. J. A. M. A. **76**:276 (Jan. 22) 1921.

In his study of pneumococcus peritonitis in infancy and early childhood, Beaven [93] concluded that this disease is in the great majority of cases preceded by pulmonary involvement, either as pneumonia or as empyema.

Nobécourt and Mathieu [94] discussed purpura occurring in pneumococcus infections of lung, intestines or meninges, and stated that the eruption is evidently an expression of septicemia, and indicates a grave prognosis.

Treatment: Isolation.—Southworth [95] considered the isolation of pneumonia cases of sufficient importance to make a plea for it the main theme of his president's address read before the American Pediatric Society in May, 1920.

Locke, Thomas and O'Hara,[68] reported in detail for the pneumonia service of the Boston City Hospital. They believed the advantages of a separate pneumonia service in a hospital include the following: The segregation of pneumonia cases greatly diminishes the danger of infection to other patients in the hospital. A separate pneumonia service facilitates the attainment of the particularly careful observation and nursing which is necessary, and also it enables the resident physicians to acquire the expert training and experience which is necessary for certain forms of treatment. Such a service also facilitates the routine special technical study required for the proper treatment of these cases, as well as research study and instruction.

Serum.—In a series of short articles on biologic therapy, the use of antipneumococcus serum was discussed by Cole.[96] Inasmuch as the pneumococci of Types I, II and III have immunologic properties of great specificity, an immune serum that will protect mice against lethal doses of any strain of pneumococci of one type will do so for all strains of that same type, but not of the other types. Consequently an immune serum has therapeutic value in man only against the strains of its particular type. The various strains in Type IV possess too high a degree of individual specificity to make an immune serum for Type IV practicable. Therapeutically effective immune serums for Types III and II have not yet been developed. But the serum of horses immunized to Type I pneumococci is of such great value in the treatment of cases of pneumonia due to Type I pneumococci, that all cases of pneumonia should be typed at once so that this serum can be used in the treatment of these cases of Type I origin. The dose of the

93. Beaven, P. W.: Pneumococcic Peritonitis in Infancy and Early Childhood, Am. J. Dis. Child. **20**:341 (Oct.) 1920.

94. Nobécourt, P., and Mathieu, R.: Purpura in the Pneumococcal Infections of the Breastfed, Arch. de méd. d. énf. **23**:689 (Dec.) 1920.

95. Southworth, T. S.: Segregation of Pneumonia, J. A. M. A. **75**:919, (Oct. 2) 1920. Also abstr. Arch. Pediat. **37**:666 (July) 1920.

96. Cole, R.: Antipneumococcus Serum, J. A. M. A. **76**:111 (Jan. 8) 1921.

serum is from 90 to 100 c.c., given intravenously, repeated every eight hours until the infection is overcome. The average total dosage is from 200 to 300 c.c., but in severe cases a total of 1,000 c.c. may be necessary. Cole added that in 495 cases of lobar pneumonia due to Type I pneumococci and treated with immune serum, there was a mortality of only 10.5 per cent.

In experimental pneumococcus Type I pneumonia in monkeys, as investigated by Cecil and Blake,[97] the intravenous injection of Type I pneumococcus serum exercises a specific therapeutic effect, frees the blood promptly and permanently from pneumococci, shortens the course of the disease and greatly moderates its severity. The earlier the serum is administrated the shorter and less severe the pneumonia. Frequent injections are also a factor in obtaining favorable results. When serum treatment is instituted late in the disease, the injections must usually be continued over a longer period of time in order to achieve success.

Locke, Thomas and O'Hara [68] reported that they had had good results with the Rockefeller Institute method of using antipneumococcus serum for Type I cases, particularly when given early, and also particularly when there was a marked thermal reaction. Cecil [97] gave a clear and instructive presentation of this serum treatment, and he also urged [64] that the bacteriologic diagnosis of each case be made early not only to determine whether or not to use serum treatment but also for prognostic value. Niles [98] felt that no patient suffering with lobar pneumonia can be said to have been given his maximum chances for recovery unless the type of infecting organism has been determined and if this proved to be Type I pneumococcus, to have received adequate doses of serum. The exceptions are: (1) young children whose intoxication is mild and in whom the difficulty of treatment is great; (2) adults first seen late in the disease, who are but mildly intoxicated and shrowing improvement, and (3) elderly patients. He urged that the serum reach the vein warmed to body temperature. Antipneumococcus serum used in the treatment of pneumococcus pneumonia in three infants of two, four, and five months of age, made a very favorable impression on Nobécourt and his associates.[71]

Gray [99] made use of Kyes' antipneumococcus serum, a serum supposedly of high antibody content, achieved by using an insusceptible host, the barnyard fowl, thereby allowing the use of unusually large

97. Cecil, R. L.: The Prevention and Serum Treatment of Lobar Pneumonia, M. Clinics N. America **4**:191 (July) 1920.

98. Niles, W. L.: The Serum Treatment of Lobar Pneumonia, New York M. J. **113**:871 (June 15) 1921.

99. Gray, A. W.: Antipneumococcus Serum (Kyes's) in the Treatment of Pneumonia, Am. J. M. Sc. **159**:885 (June) 1920.

numbers of virulent living pneumococci as antigen. As a result, the dosage of this serum was only from 2.5 to 10 c.c., given intravenously every day or two, and totalling from 60 to 90 c.c. in the cases of recovery. With this method, Gray had a mortality of 16.7 per cent. in 234 serum treated cases of pneumococcus pneumonia in soldiers and a mortality of 53.6 per cent. in 1,684 similar cases at the same time, treated in exactly the same manner except that they received no serum. No mention is made of the types of pneumococcus. However, Gray added that the modus operandi of the serum is, of course, of great interest but except for the fact that the serum is antibacterial, any statement would be hypothetical. He felt that the therapeutic value of any treatment must finally be judged by its reduction of mortality.

Management and Drugs.—Heiman [100] made a study of pneumonia in infancy and childhood, and since his mortality rate in the bronchopneumonia cases in children under one year was but 22.9 per cent., his method of treatment is of interest. He emphasized the necessity of hygienic care and efficient nursing, especially to prevent infection of the skin, eyes and mouth. Cold air treatment was not favored for any type of case. Diluted milk, gruel, fruit juices and an abundance of water form the chief elements of the food. Milk of magnesia in the morning and an enema by night are routine for purposes of elimination.

Aromatic spirits of ammonia and liquor ammonii anisatus are useful for mild stimulation and seldom upset the stomach. He also felt that whisky in doses of from 10 to 20 drops at four hour intervals helps in producing temporary stimulation and in its caloric value, and given this way has no subsequent depressing effect. Warm packs are useful in the moderately severe cases.

He did not look with favor on dry cupping and digitalis. The latter had been used in a considerable number of cases without any appreciable beneficial results, since as a rule the pulse was not lowered nor the blood pressure raised by this agent.

On the other hand, Eggleston [101] has found that in the absence of satisfactory therapeutic response, one can be certain that digitalis has been given a fair trial only when it has been administered to the point of production of one or more of the criteria of minor intoxication. Freeman [102] also said, in discussing Heiman's paper, that though for years he did not use digitalis in children, recently he had seen it do a

100. Heiman, H.: A Study of Pneumonia in Infancy and Childhood During Recent Epidemics, Am. J. Dis. Child. **20**:119 (Aug.) 1920.

101. Eggleston, C.: Some Newer Concepts in Digitalis Therapy, Am. J. M. Sc., **160**:625 (Nov.) 1920.

102. Freeman, R. G.: quoted by L. C. Schroeder in private notes.

great deal of good and he had been using it in large doses, and had found it valuable especially when given early to older children.

Brooks and Carroll [103] made a special plea for the proper management of the heart in pneumonia, believing that the most frequent immedate cause of death in all types of pneumonia is cardiac failure, which, in turn, is usually due to a deficiency of the right side of the heart. This deficiency occurs because of the very limited muscle reserve capacity of the right side of the heart, and also because of a myocardial degeneration, the result of the toxemia. They believe that small doses of digitalis at the outset of a pneumonia enable the right side of the heart to realize in the presence of an initial increased pulmonary pressure, a compensatory circulatory adjustment. Accordingly, they give the tincture of digitalis when the diagnosis is first made or even suspected.

Meakins [104] and Rudolph,[105] both advocated the administration of oxygen for the relief and prevention of anoxemia and its attendant cyanosis, in cases of pneumonia. The former used the Haldane face-mask attachment for the administration of the oxygen in satisfactory concentration, whereas Rudolph administered the gas through a rubber tube inserted into one nostril, using rhythmical compression of the opposite nostril during inspiration, the patient's mouth, of course, being kept closed.

Lassalle [106] advocated the subcutaneous injection of 1 c.c. of ether every four hours, or twice a day, the earlier in the disease the better, believing that the action of the ether is anti-infectious, antithermic, antispasmodic and cardiotonic. He had never witnessed any injurious by-effects in over 200 injections.

In ninety infants with pneumonia or capillary bronchitis, Vogl [107] made subcutaneous injections of 0.2 c.c. of a 1:1,000 solution of epinephrin with what he considered were excellent results. He believed the treatment to be logical in that it combatted the process of exudation in the finer air passages, and the infiltration of the lung tissue.

In his treatment of a case of central pneumonia in a child of 2 years, Gunewardene [83] noted benefit from aspirin and later from strychnine.

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103. Brooks, H., and Carroll, J.: The Management of the Heart in Pneumonia, Am. J. M. Sc. **160**:815 (Dec.) 1920.

104. Meakins, J. C.: The Therapeutic Value of Oxygen in Pulmonary Lesions; Preliminary Note, Brit. M. J. 324 (March 5) 1920.

105. Rudolph, R. D.: The Therapeutic Use of Oxygen, Am. J. M. Sc. **160**: 542 (Oct.) 1920.

106. Lassalle, M.: A Contribution to the Study of Bronchopneumonia in Infancy and to Its Treatment, Arch. de méd. d. énf. **23**:414 (July) 1920.

107. Vogl, J.: Epinephrin in Pneumonia in Infants, Arch. f. Kinderh. **68**: 215 (Oct. 16) 1920. Abstr. J. A. M. A. **75**:1682 (Dec. 11) 1920.

John,[108] in a description of his routine administration of glucose in pneumonia, advocated giving intravenously 250 c.c. of a 10 per cent. aqueous solution of glucose two or three times a day. He further advised the administration in the glucose solution of the various medicines needed, so that the solution usually given consists of: Tincture digitalis, 7; morphin sulphate, 0.008; atropin sulphate, 0.00064; glucose, 10 per cent. solution, 250, heated to 50 C. The administration should take from fifteen to thirty minutes. The morphin and atropin are to secure rest and also to prevent the chills which sometimes follow any intravenous medication.

Rathery and Bonnard [109] have treated cases of bronchopneumonia of the lower and middle lobes by injecting through the tissues of the neck into the trachea from 5 to 10 c.c. of 10 per cent. gomenol oil. They pass the needle in immediately above the cricoid cartilage in the midline. They stated that the results have been excellent, the injections giving immediate relief to the dyspnea, and a quick change in the state of general wellbeing. They have not had an opportunity of using this method in the treatment of bronchopneumonia of the apices.

Brooks [110] called attention to the duty of the physician not to neglect his pneumonia patients when the temperature has returned to normal, nor even when they are up and about. He considered that the physician's responsibilities and liabilities cease only when the physician has returned his patient to his usual life requirements in as normal and efficient a condition as it is possible to gain. Brooks discussed diet, hygiene and graded exercises, as well as the possible complications and sequels that might appear.

Vaccines.—Cecil [111] described the preparation, method of administration, dosage, reactions, indications for use, and contraindications for pneumococcus vaccine. He believed that prophylactic vaccination against pneumonia using a mixed saline vaccine of pneumococci Types I, II and III, to be of marked advantage where large groups of individuals are living together under abnormal conditions as in army encampments. But he advised the use of the greatest caution in recommending the treatment of pneumonia by vaccines of whatever modification, until such time as the value of these vaccines for this purpose may be confirmed by large and well controlled series of cases. He and Blake found that the subcutaneous inoculation of monkeys with pneumococcus Type I vaccine in doses comparable with those

108. John, H. J.: Glucose as an Adjunct Measure in the Therapy of Pneumonia, Am. J. M. Sc. **160**:542 (Oct.) 1920.

109. Rathery, F., and Bonnard: Intratracheal Medication in Acute Bronchopneumonia, Bull. et mém. Soc. méd. d. hôp. de Par. **44**:63 (Jan. 16) 1920.

110. Brooks, H.: The Management of Convalescence in Pneumonia, M. Clinics N. America **4**:1423 (March) 1921.

111. Cecil, R. L.: Pneumococcus Vaccine, J. A. M. A. **76**:178 (Jan. 15) 1921.

employed in man, does not protect them against subsequent attacks of pneumococcus Type I pneumonia, either spontaneous or experimental. Vaccination did, however, modify the course of the disease. Invasion of the blood stream by the pneumococci in vaccinated animals is usually slight, and the proportion of recoveries is considerably higher for vaccinated than for unvaccinated monkeys.

Howell [112] experimented with the army lipovaccine, and found apparently that immune bodies appearing after the injection of lipopneumococcus vaccines develop slowly, not reaching their height for a considerable time, and that they persist for a duration of at least several months. She further found that agglutinins, complement fixing bodies, and protective bodies for pneumococci Types I, II and III are demonstrable in the serum of individuals vaccinated with pneumococcus lipovaccine. These antibodies appear in the serum rather late and are present to some degree for at least one year.

Conclusion.—In discussing the change of type of disease, Rolleston [113] noted from the clinical viewpoint how various diseases had changed their types from one period to another, notably influenza, pneumonia and scarlet fever, and that causes for these alterations in the clinical features were appearing in modern scientific knowledge, such as the appearance of the pneumococcus and *Streptococcus hemolyticus* in measles and influenza, and the discovery of the different types of pneumococci. He believed also that changes in the resistance of the patients were important.

EMPYEMA

Pathogenesis.—Moschcowitz [114] wrote a long and elaborate but excellent paper on the newer conceptions of the pathogenesis and treatment of empyema. As to the pathogenesis, he concluded that empyema in most instances results from the rupture of a small subpleural pulmonary abscess, and is in itself the final stage of a process in which the first stage is a serous pleurisy, and the second a seropurulent pleurisy. This latter is the so-called formative stage of an empyema, and is unaccompanied by pleural adhesions, while the stage of final empyema is always accompanied by adhesions. In fact, the vast majority of empyemas are of the encapsulated variety, and very few occupy the entire pleural space. He also concluded that metastatic

112. Howell, K. M.: Blood Changes and Antibody Production in Human Beings after Injection of Pneumococcus Lipovaccine, J. Infect. Dis. **27**:557 (Dec.) 1920.

113. Rolleston, H.: The Change of Type of Disease, J. A. M. A. **74**:1495 (May 29) 1920.

114. Moschcowitz, A. V.: Newer Conceptions of the Pathogenesis and Treatment of Empyema, Am. J. M. Sc. **159**:669 (May) 1920.

suppurations accompanying empyemas are to be found rather as complications of the causative pneumonia than of the empyema.

Renaud [115] wrote that acute purulent pleurisy is always the reaction of the pleura to some lesion in the lung. The nature and the distribution of the pulmonary lesion are what determine the pleurisy, and the prognosis depends on the process in the lung.

Graham [116] made a study of the influence of respiratory movements on the formation of pleural exudates, having clinically observed the appearance of a pleural exudate of 1,000 c.c. or more in two days' time after the onset of a streptococcal bronchopneumonia. He experimented with dogs' lungs suspended in a closed bell jar, the trachea being connected by a tube with the atmosphere. He produced expansion and contraction by varying the air pressure in the jar, and noted the formation of an exudate from the surface of the lungs. He explained the exudation during inspiration as due to suction outside the visceral pleura, and during expiration as due to pressure squeezing fluid out of an oedematous pleura, there being a sudden diminution of the lung surface in expiration.

Occurrence.—Of the 1,869 cases of pneumonia admitted to the Babies Hospital in New York City in the seven years prior to Jan. 1, 1920, Spence [117] found that 204 cases, or approximately 11 per cent., either had empyema at the time of admission or developed it during the stay in hospital. All his cases of empyema were the sequel of pneumonia. Glenn [118] in her series of sixty-four cases of empyema in children under 12 years of age noted a greater incidence in males than in females (44 to 20). She also believed that the left side is more often involved than the right, her figures in this respect being 34 to 23, and the corresponding figures of Ladd and Cutler,[119] (95 to 73, with 4 bilateral) are in apparent accord. Hand [120] spoke of the rarity of empyema in colored children.

Symptomatology and Diagnosis.—Spence [117] believed the most important physical signs of fluid in the pleural cavity of the young child are flatness on percussion and displacement of the heart. The

115. Renaud, M.: The Treatment of Acute Purulent Pleurisy, Bull. et mém. Soc. méd. d. hôp. d. Par. **44**:1225 (Oct. 15) 1920; **44**:1251 (Oct. 29) 1920; 44:1334 (Nov. 12) 1920.

116. Graham, E. A.: Influence of Respiratory Movements on the Formation of Pleural Exudates, J. A. M. A. **76**:784 (March 19) 1921.

117. Spence, R. C.: Empyema in Infants and Young Children, Am. J. Dis. Child. **20**:545 (Dec.) 1920.

118. Glenn, E.: Empyema in Children: Report of 64 Consecutive Cases, New York M. J. **112**:987 (Dec. 18) 1920.

119. Ladd, W. E., and Cutler, G. D.: Empyema in Children, Am. J. Dis. Child. **21**:546 (June) 1921.

120. Hand, A.: The Diagnosis of Empyema in Children, Pennsylvania M. J. **23**:697 (Sept.) 1920.

degree of leukocytosis is no guide to either the diagnosis or the prognosis, he found. Wilcox [80] wrote that dullness or dull tympany and sharp bronchial breathing and voice sounds are found over pleuritic effusion in childhood when that effusion is in sufficient quantity to exert pressure on the adjacent lung and produce tension in the thin chest wall. Hand [120] noted that there was no one pathognomonic sign of empyema in children. He called attention, however, to the differences in the physics of the child's chest as compared to that of the adult, viz., the greater resiliency of the walls, the greater mobility of the heart, and the greater ease with which the vocal and respiratory sounds may be transmitted through effusions.

Blauner [82] found that because of the great resiliency of a child's lung, the physical signs of compression of the lung usually found in empyema, such as bronchial breathing, may be absent. In one paper Foster [66] discussed in detail the diagnosis of empyema, and disagreed with the teaching that there is always a displacement of neighboring viscera, such as of the heart or liver. In another,[121] he stated that the indications of empyema are not in signs alone at best, but in the evidence of a persistent infection, accompanied by signs in the chest which might be due to a pleural abscess.

In a child of two and a half years, Zuviria [122] found normal percussion resonance with ordinary percussion, but when the percussion was extremely gentle and the child sitting up without support except for its hands, dullness was found on the entire left side of the chest, and puncture in the ninth interspace released an effusion. The coexistence of a vesicular murmur was misleading at first.

Wessler [123] gave a number of case reports and roentgen-ray illustrations of several different varieties of encapsulated empyemata, including some particularly clear illustrations of interlobar effusions. He stated that the clinical diagnosis of encapsulation is best made when based on a consideration of all the symptoms and physical signs, though in a few cases there may be found physical signs of direct applicability.

Treatment.—Moschcowitz [114] believed that the treatment of an empyema should be begun in the formative stage before the exudate has been converted into frank pus. He wrote that it is unwise to perform an operation in this formative stage. The mortality is terrific because the accompanying pneumonia is still in full bloom, and furthermore, because of the absence of adhesions there occurs a pneumothorax with "fluttering of the mediastinum" and consequent embarrassment of

121. Foster, N. B.: The Complications of Pneumonia, Med. Rec. **99**:950 (June 4) 1921.

122. Martinez, Zuviria, E.: Prensa med., Argentina **6**:195 (Dec. 10) 1919.

123. Wessler, H.: The Diagnosis of Encapsulated Pleural Effusions, M. Clinics N. America **4**:69 (July) 1920.

the heart action. He felt that the best surgical procedure in this stage is repeated aspirations, done every twelve to twenty-four hours, in order to relieve the respiratory embarrassment due to the mechanical pressure of the rapidly accumulating fluid. He added that in a few cases this measure is curative. McCrae [124] also made a plea for the early aspiration of any pleural effusion occurring in lobar pneumonia in order to prevent, if possible, the formation of an empyema subsequently. A number of other authors, Ladd and Cutler,[119] Lowenburg,[125] Ransohoff,[126] Renaud,[115] and others, called attention strongly to the dangers of early operation for empyema, and particularly in the presence of a pneumonia. Foster [66] believed that aspiration can be continued and operation postponed as long as the patient shows improvement, as by better appetite and sleep, a lower fever and pulse rate, and other evidences of diminished infection, such as less sweating, and an improvement in the patient's sense of well being and strength. Hodge [127] also wrote in similar strain, and Renaud [115] considered the pleural complication as negligible in comparison to the condition of the lungs and heart.

Spence [117] quoted Swift as advising early operation as soon as the diagnosis has been made, since in his experience all cases in which a pleural exudate containing bacteria was obtained, ultimately came to operation. This has not been Spence's experience with infants and young children at the Babies Hospital, where in six cases, although a seropurulent fluid containing many pneumococci was obtained in small amount by aspiration, all recovered without further aspiration. However, Spence found a high net mortality rate for those cases that were treated only by aspiration since this was the only operative procedure used for the cases received in a nearly moribund condition. In this same connection but in soldiers, Abrahams [78] reported very remarkable results. In 116, or 20.8 per cent., of his cases of untyped lobar pneumonia, empyema was considered present, but aspiration was done freely and empyema diagnosed even if only a little thin serous effusion containing few pus cells was obtained. Resection was done in only thirty of the 116 cases, the other eighty-six being all successfully treated by aspiration only, although sixty showed thick pus, including twenty-four in which either pneumococci or streptococci were found. However, twenty-three deaths occurred among the thirty who were operated on.

124. McCrae, T.: The Treatment of Empyema in Lobar Pneumonia by Early Aspiration, Canad. M. A. J. **10**:162 (Feb.) 1920.

125. Lowenburg, H.: Pleural Disease in Infants and Children. With Special Reference to Empyema, New York M. J. **112**:124 (July 24) 1920.

126. Ransohoff, J.: Empyema at the Cincinnati General Hospital During the Influenza Epidemic, J. A. M. A. **74**:238 (Jan. 24) 1920.

127. Hodge, E. B.: Empyema in Children, Arch. Pediat. **38**:18 (Jan.) 1921.

As for the actual aspiration, when exploratory, Hand's [120] site of choice was the sixth interspace in the midaxillary line, preferably with the patient under general anaesthesia. After inserting the needle, he advocated in turn exploring inwards, backwards, and forwards, with only one insertion of the needle.

That thoracentesis is not entirely without danger was shown by Schlaepfer [128] who reported an instance wherein, during this operation, the needle being used for the exploratory puncture was left open as the syringe was removed. Air was aspirated and apparently drawn into a vein in the lung, for air embolism in the brain resulted, shown by loss of consciousness for 2½ hours, and total blindness for three days. He believed that air aspiration and embolism may explain many of the cases recorded as pleural shock, although in other instances slight shock on a nervous basis in the predisposed may be assumed.

An editorial [129] in the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION called attention to the possibility of a tiny droplet of air passing through a hollow needle into a pulmonary vessel during thoracentesis, and thence to a cerebral vessel causing grave symptoms, even death. It cautioned the operator to avoid this danger as by connecting the needle to rubber tubing and filling this system with saline solution.

Apert and Vallery-Radot [130] reported an instance of sudden death during thoracentesis in a 4 year old boy who was terribly frightened and violently resisted the puncture which had to be done twice while the patient was firmly held by a nurse. Fatal syncope suddenly occurred. At necropsy, a myocarditis was found which was thought to have been diphtheritic since any other kind in a child of four is rare. The boy had been sick a month, and had developed a bilateral serous effusion, but there were no symptoms suggestive of diphtheria.

Villandre [131] believed that before operating in a case of purulent pleurisy, a great deal more attention should be paid to the bacteriology than is usual. He felt that the pneumococcus cases may, but the streptococcus cases always require incision, the latter almost always requiring in addition the use of surgical solution of chlorinated soda, or of an antiseptic vapor, for the best results. He presented an excellent description of the various methods of treatment. Foster [122] spoke of

128. Schlaepfer, K.: A Case of Three Days' Blindness after Diagnostic Puncture of the Lung, Deutsch. Ztschr. f. Chir. **159**:132 (Sept.) Abstr. J. A. M. A. **76**:828 (March 19) 1921.

129. Editorial: Air Embolism Following Thoracentesis, J. A. M. A. **76**:1314 (May 7) 1921.

130. Apert, and Vallery Radot, P.: Sudden Death During Puncture of Pleura in a Child of 4 years. Myocarditis, Bull. et mém. Soc. méd. d. hôp. de Par. **44**:852 (June 18) 1920.

131. Villandre, C.: The Treatment of Acute Purulent Pleurisies, Bull. méd. Par. **34**:87 (Jan. 31) 1920.

the danger of early operation in streptococcus empyema, and thought it better to aspirate as long as this procedure gave improvement in symptoms. He felt, however, that often a pneumococcus empyema was benefitted by early operation. Spence [117] noticed that when the pus yielded a pure culture of pneumococcus, the mortality was lowest; but when there was a mixed infection or a pure growth of streptococcus, the mortality was highest.

Spence further noted that the length of time since the onset of symptoms also seemed of importance in the prognosis. If short, the mortality was high from overwhelming or virulent infection; if from two to six weeks, the mortality was lowest; if over six weeks, the mortality was again high from neglect or complications. Locke [132] called attention to the fact that the earlier the empyema occurred in the course of a pneumonia, the worse was the prognosis. Also, the prognosis of empyema with lobar pneumonia is much more favorable than with bronchopneumonia. Glenn [118] thought that when the patient is operated on within the first week after the onset, the average stay in the hospital is shorter and the proportion of cures higher than in those operated on at the later time.

Operative Treatment.—A detailed review of the literature on this branch of the subject is not indicated at this time. Accordingly only a few points from various of the papers will be noted here.

Moschcowitz [114] stated that the treatment in the acute stage of an empyema consists of a simple intercostal thoracotomy, an operation which need not be considered urgent, and which should be performed when the patient's condition is otherwise perfectly satisfactory. Urgent thoracotomy is indicated only in acute pyopneumothorax. He felt that the Carrel-Dakin treatment, properly carried out, has proved of superlative value in the postoperative treatment of empyema and should be used in every case. There are no contraindications to its use, and the mortality of acute empyema treated by these methods is lower than that reported by other methods of treatment, he found. Empyema cavities heal by three methods: (1) by the formation and absorption of a sterile exudate; (2) by the formation and "absorption" of a closed pneumothorax, and (3) by the "classical" method, i. e., the expansion of the lung and obliteration of the pleural cavity by adhesions. Chronic empyema should not occur, or at least should become very rare, if the methods of treatment of acute empyema formulated above are practised. Wilensky [133] wrote in much the same strain. Ransohoff [126] felt that flushing of the cavity with surgical solution of chlorinated

132. Locke, E. A.: Empyema Complicating Pneumonia, M. Clinics N. America **4**:471 (Sept.) 1920.

133. Wilensky, A. O.: Present Status of Empyema, Am. J. M. Sc. **160**:384 (Sept.) 1920.

soda or other solution is unnecessary, except when defervescence does not occur, indicating that spontaneous sterilization of the cavity is not progressing normally. He thought that operation not earlier than the end of the second week gave the best results, and that rib resection is indicated only when sufficient space is not at command without it. He favored some type of the occlusion method of operation by which the entrance of air into the pleural cavity is prevented and the exit of pus facilitated. A suction apparatus attached to the tube was deemed unnecessary. Spence [117] stated, however, that in the experience of the Babies Hospital, siphon drainage has given better results in the treatment of empyema in infancy than any other treatment employed.

Ladd and Cutler [119] remarked that whereas children do not stand rough handling and hemorrhage as well as adults, the lung can be freed gently, sufficiently to allow it to expand without causing marked bleeding. In the streptococcus infections, these authors felt that aspiration or closed drainage through a tube would probably supply sufficient drainage and result in a lowered mortality. In cases of pneumococcus empyema, they considered closed drainage useful as a temporary measure for the extremely sick patients, but not to be recommended as the operation of choice. It does not supply adequate drainage nor allow the operator to free the lung which can be done in a child through a small opening with one finger. They considered the cause of collapsed lung to be not the presence of atmospheric pressure through an open wound, but the result of inadequate operation and drainage.

Rosenberg [134] recommended the open pleura puncture of Schmidt in cases in which the exudate extends beyond the upper third of the scapula or when no resorption takes place after two or three weeks. The method consists mainly in replacing the exudate with air, thereby preventing the redevelopment of exudate and the formation of broad adhesions between the costal and visceral pleura.

Morrison [135] reported a case of a 2½ year old girl with a left-side Type I pneumococcus empyema following lobar pneumonia, but complicated by whooping cough. Under procain local anesthesia, he resected part of the eighth rib through an incision made over the ninth rib, believing that an indirect opening into the pleural cavity is much better than a direct one in that it prevents air rushing in and out of the pleural cavity with each respiration. A valve fashioned from the soft tissues themselves is more efficient than any mechanical valve, and he also considered that general anaesthetics are contraindicated. In

134. Rosenberg, M.: Exudative Pleurisy, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **32**:267, 1920. Abstr. J. A. M. A. **75**:1684 (Dec. 11) 1920.

135. Morrison, W. R.: Acute Empyema Complicated by Whooping Cough, Boston M. & S. J. **184**:307 (March 24) 1921.

another article [136] he gave a more detailed description of the operative technic of this operation.

Moschcowitz [114] considered that feeding with a diet rich in calories was a valuable adjuvant in the treatment particularly of the formative stage. Locke [132] also laid stress on the necessity of giving consideration to the diet in order to avoid, if possible, the rapid and marked emaciation which is so common in empyema, and he urged that the patient be encouraged to take a special dietary having a fuel value of from 3,000 to 3,500 calories. He also advocated the open air treatment whenever possible. Hodge [127] called attention to the value of blowing exercises started as early as possible in order to expand the lung.

Gay and Morrison [137] experimented with various dye stuffs in the treatment of experimental streptococcus empyema in rabbits, and stated that their results did not justify the anticipation of practical therapeutic results from the use of dye stuffs in empyema due to the streptococcus. They added, however, that they have not as yet considered the possibilities of using dyestuffs combined with metallic compounds such as with mercury. Gay and Stone [138] made elaborate experiments on animals with a strain of streptococcus isolated from a case of human empyema, and concluded that preventive vaccination against human streptococcus empyema was not practicable, and that therapeutic results in animals with such vaccines were consistently negative. On the other hand, Dufour and Debray [139] reported the recovery from a streptococcus purulent pleurisy under the influence of vaccine therapy alone, of a girl of 15 in whom the disease had developed slowly and the general health was good.

After a study of twenty-two cases of pneumococcus empyema in children with particular reference to demonstrable precipitins in the exudate, Floyd [140] suggested that pleural irrigation with an appropriate immune serum be used as a means of treatment of this disease in order to increase locally the immune substances that tend to limit the duration of the disease. He further noted that the pleura will clear itself of

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136. Morrison, W. R.: The Surgical Treatment of Acute Empyema by Valve Drainage, Provided by Flap of Skin, Fascia and Muscle, under Local and Paravertebral Anaesthesia, Boston M. & S. J. **182**:366 (April 8) 1920.

137. Gay, F. P., and Morrison, L. F.: Experimental Streptococcus Empyema: II. Attempts at Dye Therapy, J. Infec. Dis. **28**:1 (Jan.) 1921.

138. Gay, F. P., and Stone, R. L.: Experimental Streptococcus Empyema: Attempts at Prevention and Therapy by Means of Vaccines and Serum, J. Infec. Dis. **26**:265 March) 1920.

139. Dufour, H., and Debray: Vaccine Treatment of Purulent Pleurisy, Bull. et mém. Soc. méd. d. hôp. de Par. **45**:16 (Jan. 14) 1921. Abstr. J. A. M. A. **76**:896 (March 26) 1921.

140. Floyd, C.: A Study of the Precipitin Test in Cases of Pneumococcus Empyema, J. Immunol. **5**:321 (July) 1920.

a pneumococcus infection in a much shorter time than the average if the secondary invaders can be excluded.

Chronic Empyema.—Cauchoix [141] stated the causes of chronic empyema to be (1) incomplete drainage; (2) the presence of a foreign body; (3) the presence of an osteitis of a rib, and (4) other conditions, often undeterminable. He studied the various ways of treating this form of the disease, and believed that much help can be obtained from the use of irrigation with surgical solution of chlorinated soda. Moschcowitz [114] stated that chronic cases of empyema may be defined as such which are not amenable to treatment by the Carrel-Dakin method, but he also felt that chronic empyema should not occur, or at least should become very rare, if this method is used in the treatment of the acute cases.

Gordon [142] made a study of cases of chronic empyema at Camp Gordon which for the most part were originally caused by the hemolytic streptococcus, and found that these hemolytic streptococci played a minor part in those empyemata which developed into a chronic state. For long after these microorganisms were demonstrated to be absent from cultures from the wounds or from the secondary operative fluids, fetid purulent discharges continued to be given off, and closure of the wound was impossible. Furthermore, a high degree of immunity to the hemolytic streptococcus was demonstrated in these cases. On the other hand, a heterologous group of proteolytic bacilli, of which one group predominated, was observed in a large percentage of the cases. A variety of the proteus group was isolated from these secondary invaders, but the predominating organism among them in his series was a gram negative bacillus broadly belonging to the Friëdlander group. The typical bacterial picture which he found in his cases of empyema accordingly showed the following sequence: (1) hemolytic streptococci in pure culture; (2) the gradual supplanting of the streptococci by a flora of secondary invaders, and (3) the freeing of the wound of these organisms under treatment, followed by closure.

Gordon further noted that the blood picture of chronic empyema, in contradistinction to acute cases in which the leukocytosis is high with a high percentage of polymorphonuclear ecIls, gives a low grade leukocytosis of about 10,000 cells per cubic centimeter, and a neutrophilia of from 60 to 70 per cent. A secondary anemia is invariably present in old and protracted cases.

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141. Cauchoix, A.: A Discussion of the Causes and of the Evolution of the Treatment of Chronic Empyema, Bull. méd., Par. **34**:91 (Jan. 31) 1920.

142. Gordon, J. E.: The Bacteriology of Chronic Empyema, J. Infect. Dis. **26**:29 (Jan.) 1920.

Hirsh [143] reported a case of chronic empyema prolonged by osteomyelitis of several partially resected ribs, as being greatly benefitted by "diathermy," the peculiar current derived from a high frequency apparatus constructed just for this purpose. d'Heucqueville [144] showed by pneumographic tracings the advantage of deep respirations in helping to break up pleural adhesions. The after treatment for nonexpanded or partly expanded lung tissue, Goetze [145] claimed, is helped tremendously by the use of a mask so constructed that a valvelike adjustment, while permitting easy inspiration, makes expiration more difficult.

BRONCHIECTASIS, LUNG ABSCESS, AND PULMONARY GANGRENE

Elliott [146] reviewed forty cases of dilatation of the bronchi that he saw in one year, seven of them being in children. He noted that hemorrhage is frequent and may be slight or severe; also that clubbing of the fingers and toes is a very suggestive symptom, being noted as present in twenty-two of the forty cases, and possibly present in more. Nutrition was usually good and was of some assistance in differentiating from tuberculosis.

Menétrier and Durand [147] reported in detail a case of brain abscess which occurred apparently secondary to chronic bronchiectasis. At necropsy chains of streptococci were found in smears made from the brain abscess and from the bronchiectatic cavities.

In a discussion of the bronchoscopic treatment of bronchiectasis and lung abscess, Lynah [148] stated that although pulmonary drainage is difficult in all cases of circumscribed abscess, he believed the conservative bronchoscopic measures of treatment should be given a thorough trial first, before radical major surgery is attempted.

In another paper, Lynah [149] described his roentgenographic studies of bronchiectasis and lung abscess. He sterilized by boiling a 1:2 mixture of bismuth subcarbonate in pure olive oil, and slowly injected 8 c.c. of this mixture through a bronchoscope into the bronchi and

143. Hirsh, A. B.: Diathermy an Aid in Empyema, Med. Rec. **98**:1015 (Dec. 18) 1920.

144. d'Heucqueville, R.: Pneumography of Pleural Adhesions, Presse méd. **29**:164 (Feb. 26) 1921. Abstr. J. A. M. A. **76**:1136 (April 16) 1921.

145. Goetze, O.: Differential Pressure Mask for Empyema, Zentralbl. f. Chir. **47**:29 (Jan. 10) 1920.

146. Elliott, J. H.: Dilatation of the Bronchi: A Review of 40 Cases Observed June 1918—June 1919, Med. Rec. **98**:253 (Aug. 14) 1920.

147. Menétrier, P., and Durand A.: Brain Abscess at a Site Determined by Previous Trauma in a Case of Bronchiectasis: Development Suggesting Cerebrospinal Meningitis, Bull. et mém. Soc. méd. d. hôp. de Par. **44**:1066 (July 23) 1920.

148. Lynah, H. L.: Bronchoscopic Treatment of Bronchiectasis and Pulmonary Abscess, Med. Rec. **97**:215 (Feb. 7) 1920.

149. Lynah, H. L., and Stewart, W. H.: Roentgenographic Studies of Bronchiectasis and Lung Abscess after Direct Injection of Bismuth Mixture Through the Bronchoscope, Am. J. Roentgenol. **8**:49 (Feb.) 1921.

lungs of a living patient and apparently without danger. He considered the procedure of value in mapping out bronchiectatic and lung abscess cavities. In the first five cases, no harm was done the patients; in fact, the injections seemed to be of therapeutic benefit. The bismuth apparently is afterward got rid of gradually except where it has infiltrated the lung.

Clendening [150] noted that in the last few years lung abscesses after tonsillectomies have become more frequent than hitherto. He believed that there are four possible causes: (1) inspiration of infected material; (2) the use of motordriven anesthesia apparatus, creating a positive pressure in the pharynx; (3) metastatic infection through the lymphatics; (4) swabbing or tampering with the throat after enucleation has been accomplished.

Wessler and Schwarz [151] described fifteen cases of lung abscess in infants and children, of which three followed the aspiration of a foreign body; five were subsequent to tonsillectomy, and seven were due to pneumonia or some other inflammatory condition. These authors emphasized the value of the roentgen ray not only for diagnosis but also for careful and exact oversight in the prognosis of these cases.

Foster [121] told of a case of lung abscess, treated by artificial pneumothorax to collapse the lung, which came to necropsy six years later, after death from chronic nephritis. There had been a symptomatic cure of the lung abscess but peculiar physical signs had persisted, and "radiographs were useless, the involved area being covered by the heart shadow. At necropsy, the area of the abscess was found entirely replaced by dense fibrous tissue. The healing, in brief, had been perfect."

Netter [152] reported the recovery of a boy from pulmonary gangrene under treatment with antigangrene serum made with the perfringens, the septic vibrio, and the malignant edema bacillus.

FOREIGN BODIES IN THE TRACHEA AND BRONCHI

Graham [153] wanted to enlist the interest of all pediatricians in the question of foreign bodies in the lungs or larger air passages, since 66 per cent. of foreign body cases are in children and many are undoubtedly overlooked. He stated that he suspects a foreign body in the lung if the following conditions are present: (1) localized lung

150. Clendening, L.: The Cause of Abscess of the Lung after Tonsillectomy, J. A. M. A. **74**:941 (April 3) 1920.

151. Wessler, H., and Schwarz, H.: Abscess of the Lungs in Infants and Children, Am. J. Dis. Child. **19**:137 (Feb.) 1920.

152. Netter: Pulmonary Gangrene, Bull. et mém. Soc. méd d. hôp. de Par., **45**:629 (May 6) 1921. Abstr. J. A. M. A. **76**:1862 (June 25) 1921.

153. Graham, E. E.: Foreign Bodies in the Air and Food Passages, Am. J. Dis Child. **19**:119 (Feb.) 1920.

symptoms which persist in spite of treatment; (2) no tubercle bacilli in the sputum; (3) a leukocytosis for which there seems no definite reason, and (4) gradual failure in weight and health. The symptoms vary greatly; a peanut kernel almost immediately sets up a severe laryngitis, tracheitis, and bronchitis, known as arachidic bronchitis, while a metal object may remain in a long time and do comparatively little damage.

Jackson, Spencer and Manges,[154] discussed the diagnosis and localization of nonopaque foreign bodies in the bronchi, especially nut kernels, coffee berries, and maize beans, noting that while the roentgenogram usually failed to show such a foreign body itself, nevertheless it yielded three characteristic roentgenographic signs: (1) increased transparency over the entire affected side; (2) depression of the diaphragm on the affected side, and (3) displacement of the heart and mediastinal structures away from the affected side; in short, an acute obstructive emphysema. With the later development of abscess or of "drowned lung," distinct shadows of the pathologic condition may allow the definite localization of the nonopaque foreign body but then it may be too late. And, furthermore, the possibility of the shifting of the foreign body must always be kept in mind.

These same authors mentioned the following clinical features as helpful in localizing a foreign body: (1) the unobstructed side of the chest is fuller, harsh breathing is heard, and in the arachidic cases, is accompanied by very loud snoring snapping and bubbling râles; (2) the obstructed side has less expansion, has muffled tympanic resonance, and the breath sounds have a diminished intensity; (3) the intercostal spaces on the affected side may be retracted during inspiration. The signs, of course, may be considerably altered later. Dullness to flatness may intervene due to the accumulation of secretions in the air passages below the obstruction, a condition which has been termed "drowned lung."

The signs of foreign body which McCrae[155] considered of most value are the decreased expansion on the affected side, the presence of very fine râles, and the "asthmatoid wheeze." Graham, and Jackson and his co-workers, also emphasized the value in the diagnosis of the presence of a foreign body, of this sign, the "asthmatoid wheeze," which had been previously described by Jackson in 1918. McCrae wrote that it can be heard by placing the ear or the bell of the stethoscope close to the patient's mouth. It may be found with both inspira-

154. Jackson, C.; Spencer, W. H., and Manges, W. F.: The Diagnosis and Localization of Nonopaque Foreign Bodies in the Bronchi, Am. J. Roentgenol. **7**:277 (June) 1920.

155. McCrae, T.: The Physical Signs of Foreign Bodies in the Bronchi, Am. J. M. Sc. **159**:313 (March) 1920.

tion or expiration but sometimes is only audible at the end of forced expiration. It differs from the wheezing sounds heard with bronchial asthma but this difference is difficult to describe in words, he found. The sound varies in pitch and loudness depending on the character of the foreign body causing it. McCrae had never heard it over the chest wall.

Imperatori [156] reported six unusual cases of foreign bodies in the bronchi and commented on the frequency with which radiographs would have given the cause of obscure symptoms and prevented mistaken diagnosis.

RETROPHARYNGEAL ABSCESS

Friedman and Greenfield [157] believed that retropharyngeal abscess is of comparatively frequent occurrence though often overlooked. The disease consists of a suppurative lymphadenitis of the retropharyngeal glands situated on each side of the median line between the posterior pharyngeal wall and the aponeurosis covering the bodies of the cervical vertebrae. These glands drain the pharynx, postnasal spaces, Eustachian tubes and middle ears, and hence in infection of the various structures in these localities, they partake of the infection as do lymph glands in other parts of the body. Because of the usual atrophy and disappearance of the retropharyngeal glands at or about the fifth year, the process is rare except in young children. In the majority of their cases, the source was diseased tonsils and adenoids though frequently the disease can be attributed to a purulent rhinitis. They stated that the most pronounced clinical manifestations are those resulting from obstruction, the mechanical interference occasioned by the pressure of the mass in the pharynx. "When in the first year of life an infant ceases to suck well, chokes, coughs and is restless in sleep, we should always think of a retropharyngeal abscess." When a child has a rigid neck, or is suffering from hoarseness or from the various forms of croup, a careful examination of the pharynx is called for. The only possible way, these authors felt, of confirming or ruling out a diagnosis or retropharyngeal abscess is by palpation with the finger. They urged an early and adequate vertical incision in the faucial fluctuating mass with a bistoury, followed by finger exploration, and inversion of the child.

In a very recent article, Frank [158] has given an excellent exposition of the features of retropharyngeal abscess, discussing the anatomy,

156. Imperatori, C. J.: Foreign Bodies in Esophagus and Bronchi; 6 Cases, New York M. J. **113**:438 (March 16) 1921.

157. Friedman, J., and Greenfield, S. D.: Retropharyngeal Abscess; an Experience with 60 Cases, New York M. J. **113**:604 (April 20) 1921.

158. Frank, Ira: Retropharyngeal Abscess, J. A. M. A. **77**:517 (Aug. 13) 1921.

pathology, symptomatology, diagnosis, treatment, etc., of the disease. He brought out points similar to those mentioned above.

MISCELLANEOUS

Levy [159] collected from the literature twenty-one cases of congenital absence of one lung, and reported a twenty second case, with necropsy. Twelve of the cases died during the first year of life, but the other ten lived from ten to seventy years and then often came to necropsy for other than pulmonary conditions. Hence life is not incompatible with only one lung. There seemed to be a definite predilection for this anomaly for the left side, the ratio to the right side being two to one.

Cohen [160] classified the causes of cyanosis in the newborn as: (1) the character of the labor, the cyanosis being indicative of a real asphyxia, or due to intracranial hemorrhage. (2) Developmental causes, such as *a*, pulmonary atelectasis; *b*, congenital heart defects; *c*, thymus hyperplasia; and *d*, diaphramatic hernia and other rare congenital anomalies. (3) Sepsis.

Faber [161] noted the exceptional rarity of subcutaneous emphysema occurring spontaneously during the first days of life, and could find only two such cases reported in the literature, both being fatal cases reported by Guillot in 1853. Faber reported the case of an infant who developed a marked subcutaneous emphysema on the third day of life, following apparently a marked effort to breathe while lying on the face, with resulting alveolar rupture, perhaps due to a considerable negative or positive pressure on delicate lung tissue. The baby was treated by very careful and watchful nursing, the instructions being to avoid all crying if possible. The avoidance thereby of excessive increases in intrapulmonic pressure was sufficiently complete to allow air absorption to proceed at a greater rate than air escape, and so to permit the recovery which took place.

In a study of physical defects in two groups of children, Emerson [162] noted that malnutrition, faulty teeth, postural defects, and mental backwardness were all apparently more common in children who suffered from nasopharyngeal defects than in those who had no such defects. However, in one of the groups of children studied, only 4 per cent. or presumably fourteen children were without nasopharyngeal defects so that percentages based on that number are hardly com-

159. Levy, C. S.: Congenital Absence of One Lung, Am. J. M. Sc. **159**: 237 (Feb.) 1920.

160. Cohen, F.: Cyanosis in the New Born, Arch. Pediat. **37**:666 (Nov.) 1920.

161. Faber, H. K.: Subcutaneous Emphysema in an Infant 3 Days Old, Am. J. Dis. Child. **19**:388 (May) 1920.

162. Emerson, W. R. P.: Physical Defects in Children, Report of 602 Cases, Am. J. Dis. Child. **21**:282 (March) 1921.

parable with percentages based on the other 96 per cent., or 343 children.

Fischer [163] reported the case of a 7 months old infant, who while playing with a box of dusting powder consisting chiefly of stearate of zinc, got a considerable quantity in his mouth. In twenty-four hours there were marked signs of respiratory obstruction, apparently in and around the larynx. Steam inhalations and emetics were without avail but stimulating expectorants, chiefly senega, proved successful and a recovery was made within three days.

Barnett [164] gave a short report of a 10 months old infant who poured half the contents of a jar of stearate of zinc down her throat. She immediately became cyanotic and limp and was stuporous at intervals. She developed a short hacking cough. The next day the temperature went up to 101⅗ F. and diffuse fine râles were heard over both lungs, but four days later all signs had disappeared.

D'Oelsnitz and Carcopino [165] described the cases of two children, aged 2 and 3 years, respectively, with sudden development of suffocation presumably due to enlarged tracheobronchial glands affected by a wave of congestion or inflammation. Subsidence through the influence of the roentgen ray was almost as sudden as the onset.

In his discussion of the diagnosis and significance of tracheobronchial adenopathy, Balyeat [166] stated that he considered the d'Espine sign positive if a distinctly tracheal voice is heard below the seventh cervical vertebra in children less than 3 years of age, or below the first dorsal in children between 3 and 5, or below the third dorsal in children over 5. After analysing 449 cases, which were studied in whole or part by means of symptoms, signs and roentgen-ray findings, he drew a number of conclusions, among which were the following statements: A positive d'Espine is indicative of enlarged glands at the root of the lungs. This enlargement may be due to any one of several causes, the chief of which is an infection with the tubercle bacillus. When found in a poorly nourished child this sign usually is evidence of a tuberculous infection of the hilum. Chronic bronchitis will produce enlarged tracheobronchial glands which can be differentiated from a tuberculous hilum by means of the roentgen ray. If tonsillitis, whooping cough, or measles causes enlarged tracheobronchial glands,

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163. Fischer, L.: Partial Asphyxiation in an Infant Resulting from the Inhalation of a Dusting Powder, Med. Rec. **98**:1027 (Dec. 18) 1920.

164. Barnett, N.: Insufflation of Stearate of Zinc, with Recovery, Arch. Pediat. **38**:53 (Jan.) 1921.

165. D'Oelsnitz and Carcopino: Tracheobronchial Adenopathies, Bull. et mém. Soc. méd. d. hôp. de Par. **45**:297 (March 4) 1921. Abstr. J. A. M. A. **76**:1281 (April 30) 1921.

166. Balyeat, R. M.: Diagnosis and Significance of Tracheobronchial Adenopathy, J. A. M. A. **76**:988 (April 9) 1921.

they are usually not of sufficient size or density to give a positive d'Espine.

Kernan [167] cited six cases in which bronchoscopy or esophagoscopy was instrumental in establishing the diagnosis of enlarged tracheobronchial glands, aneurysms of the aortic arch, neoplasms, etc. He advocated the more extensive employment of this diagnostic aid, especially in the hands of a skillful operator.

Imperatori [168] gave an outline of the symptoms due to lesions of the upper air passages and esophagus in which he believed endoscopy is of sufficient diagnostic value to warrant its habitual use. The opportunities for the use of the endoscope are apparently numerous.

Norris [169] believed that the roentgen ray can give information as to chest conditions with greater certainty than physical signs can, though it often does not do so. Proper team work and correlation of the facts are necessary. He urged that the radiologist be kept informed as to the clinical facts of the cases.

After an extensive review of the literature, Schlomovitz [170] concluded that pulmonary edema can be caused by the following factors: (1) The experimental production of pulmonary emboli. (2) Injury to pulmonary capillaries, either from within the vessels or from without. "The inflammatory type of pulmonary oedema which Sahli insisted on as the chief type in man, might be considered as a combination of intravascular and extravascular injury." (3 When the mechanical efficiency of the left ventricle is reduced to a greater extent than that of the right ventricle. (4) Combinations of causes.

Hoover [171] discussed the various abnormalities of movement of the inner and outer portions of the costal margins during inspiration. He noted that these movements are modified with changes in the curve of the plane of the diaphragm caused by paresis of either the diaphragm or the intercostal muscles or by synechia between the diaphragm and the thoracic wall. He believed that such studies improve the accuracy with which one differentiates between infraphrenic and supraphrenic disease, and also enable both the estimation of the conformation of the heart and the size of the pericardial sack, and the differentiation between lesions which cause phrenic displacement and those which do not modify the plane of the diaphragm.

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167. Kernan, J. D., Jr.: The Use of the Bronchoscope in the Diagnosis of Tumors of the Mediastinum, New York State J. M. **21**:115 (April) 1921.

168. Imperatori, C. J.: Endoscopy as a Diagnostic Aid in Diseases of the Upper Air Passages and Esophagus, New York State J. M. **21**:86 (March) 1921.

169. Norris, G. W.: Physical Diagnosis versus the X-ray in Disease of the Lungs, New York M. J. **112**:841 (Nov. 27) 1920.

170. Schlomovitz, B. H.: Experimental Pulmonary Edema, Arch. Int. Med. **25**:472 (April) 1920.

171. Hoover, C. F.: The Diagnostic Significance of Inspiratory Movements of the Costal Margins, Am. J. M. Sc. **159**:633 (May) 1920.

In a study of forced respiration and the experimental production of tetany, Grant and Goldman [172] noted that forced respiration in the human subject causes symptoms of tetany to occur, including carpopedal spasm, Chvostek's sign, Trousseau's sign, Erb's sign, and in one instance a tetanic convulsion. As a result of the fall of alveolar carbon dioxid tension produced by overventilation, there is a reduction in the H ion concentration of the blood, a reduction of the carbon dioxid capacity of the plasma, a change in the reaction of the urine to the alkaline side, a decreased excretion of ammonia, and a slight increase in the calcium content of the serum. They believed that the underlying factor in the tetany of forced respiration is the alkalosis.

Gerstley [173] called attention to the necessity to consider not the disease alone nor even the disease and the patient alone, but the disease, and the patient, and the environment and living conditions. In illustration he cited the case of an 8 year old boy who because of a persistent dry hacking cough of some months' duration, had been to various physicians, had taken quantities of medicines, and even had been under the care of a Christian Science practitioner. There was nothing exceptional in the general history and physical and laboratory examinations. The chest itself was negative. The dry hacking nature of the cough suggested a nervous element. The father was somewhat neurotic. Further investigation disclosed that the parents were greatly worried about the condition and spoke constantly of the cough in the boy's presence. They had kept him indoors for some weeks, and, to cause him to relax, had given him a hot bath every night. To overcome the nervous element, parents and child were advised to forget the cough entirely. All medicine was stopped. The general measures to be taken were entirely those of building up the boy's resistance. In favorable weather he should go outdoors. He should have abundant rest and good food. Hot baths were to be replaced gradually by tepid, and later cool sponges. Within two weeks the boy was well.

In another case, Gerstley noted that a chronic cough was due to the child's mimicking of a nurse clearing her throat.

ASTHMA AND HAY-FEVER

Rackemann [174] noted the great variability of asthma and how it is frequently the result of a chronic bacterial infection of the bronchi superimposed on a long-standing foreign protein sensitization. He analyzed 534 cases in the following chart:

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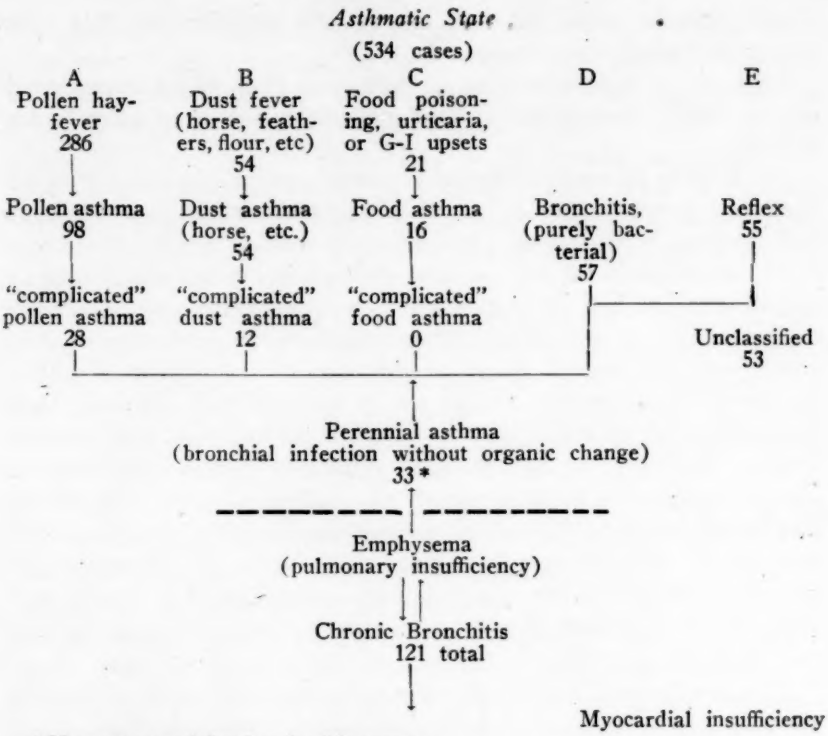
172. Grant, S. B., and Goldman, A.: A Study of Forced Respiration: Experimental Production of Tetany, Am. J. Physiol. **52**:209 (June) 1920.

173. Gerstley, J. R.: The New Era in Pediatrics, J. A. M. A. **76**:1633 (June 11) 1921.

174. Rackemann, F. M.: The Vaccine Treatment of Asthma, M. Clinics N. America **4**:1751 (May) 1921.



* New cases originating in this group.

For a classification of asthma as it occurs in infancy and children, Schloss,[175] in his classical description of allergy in infants and children, noted two of the clinical types of allergy in which asthma is a feature. The first is the hyperacute type with urticaria, asthma, and symptoms of shock. This is most commonly due to milk or egg, occasionally to beef. It is also observed in susceptible individuals after the injection of horse serum. All the symptoms usually appear within a few minutes, as after the injestion of a particular food. Usually very little of the food is actually injested as the infant spits it out of his mouth or vomits immediately after it has been swallowed. Within a few minutes there is a swelling of the lips, tongue, and buccal mucous membrane. Symptoms of collapse occur, and the patient becomes drowsy or somnolent; shortly afterward, there is marked general urticaria. Asthma commonly occurs immediately after the food is swallowed and is usually severe. It occurs in many cases but not in all. It may be absent in the earlier attacks, but present in later ones. Sneezing and conjunctival congestion are usually pronounced. The severe symptoms

175. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**:433 (June) 1920.

usually subside within an hour or two, the urticaria may last from sixteen to twenty-four hours.

The second type according to Schloss is bronchial asthma, which may be due to the proteins of food, pollens, epidermis of animals, and bacteria.

In a study of sensitization in bronchial asthma, Caulfield [176] developed two general impressions: (1) Bronchial asthma is a syndrome with quite wide variations. It frequently requires a very broad type of investigation if all the possible etiological factors which may be operative in the individual case are to be considered, and (2) despite the fullest type of investigation there will remain a percentage of cases which one must regard as typical examples of true bronchial asthma but for which no definite etiology can be demonstrated. Between these cases and those in which protein sensitization has been clearly established, there may be no detectable difference except that they are protein negative (to between seventy and eighty proteins). He thought that among some of the patients presenting the syndrome of bronchial asthma, and as well in a very large majority of hay-fever patients, there is evidence that the lesion is an immunologic one, closely analogous to, if not identical with, the experimentally produced phenomenon called anaphylaxis.

Coke [177] believed that half the cases of asthma can be proved by skin reactions to be due to some foreign protein. He wrote that asthma, hay-fever, urticaria, eczema, migraine, epilepsy and paroxysmal hemoglobinuria, have many common traits, and will probably all be proved eventually to be symptoms of anaphylaxis and not separate diseases at all.

Rackemann,[178] on the other hand, suggested that hay-fever may depend on a mechanism which is not anaphylactic but which is perhaps closely associated with that of drug idiosyncrasies.

From his personal observations on 150 cases of bronchial asthma, Piness [179] concluded that heredity is an important predisposing but not exciting factor in from 25 to 50 per cent. of the cases. By means of cutaneous tests he found it possible to determine the etiology in from 47 to 50 per cent. of the cases, and multiple sensitization was common, especially in the food and pollen groups. Sensitization to one protein in early life seemed apt to be followed by sensitization to other proteins

176. Caulfield, A. H. W.: Sensitization in Bronchial Asthma and Hay-Fever, J. A. M. A. **76**:1071 (April 16) 1921.

177. Coke, F.: Asthma and Anaphylaxis, Brit. M. J. **1**:372 (March 12) 1921. Abstr. J. A. M. A. **76**:1045 (April 9) 1921.

178. Rackemann, F. M.: The Specific Treatment of Hay-Fever, Boston M. & S. J. **182**:295 (March) 1920.

179. Piness, G.: Etiology of 150 Cases of Bronchial Asthma, California State J. Med. **19**:29 (Jan.) 1921.

but patients with a history of onset past thirty-five years of age rarely give positive skin reactions, he noted. His final conclusion was that endocrine dysfunction bears a prominent part in the etiology of asthma, particularly in the young individuals, and should be borne in mind where the patient does not respond to specific protein therapy.

In a clinical discussion of the diagnosis and treatment of asthma, hay-fever, and allied conditions, Rackemann [180] called particular attention to the importance of a careful history and a complete physical examination.

Alexander and Paddock,[181] in their study of the response to pilocarpin and epinephrin of patients with bronchial asthma, found that in a series of such cases a general examination with routine laboratory aids and drug tests revealed no constant associated condition, but the most frequent finding was abnormally increased sensitiveness to pilocarpin. The majority of cases reacted also to epinephrin with an abnormal rise in blood pressure and other characteristic signs—pallor, tremor, sometimes rigor, denoting increased sensitiveness to this drug. A relation between low blood pressure and this excessive epinephrin reaction was apparent, while the smaller number of cases with normal or high blood pressure gave regularly normal reactions. The former cases, those reacting excessively to epinephrin, were found to be relieved by 0.25 c.c., a much smaller dose of the drug than is usually employed.

Both Shambaugh [182] and Jesberg [183] called attention to the fact that asthma is often associated with definite pathologic changes in the nasal cavity. Shambaugh stated that the pathologic condition associated with most cases of asthma was a hyperplastic ethmoiditis, and he found that a correction of this condition had a very decided influence on the asthma. The relation between the nasal condition and asthma appeared to be not so much one of a nasal reflex neurosis as an anaphylactic reaction, but he felt that the improvement in the asthma resulting from operations in the ethmoid may be due to the elimination of foci harboring bacteria and their toxins.

Jesberg [183] thought that the nasal disorders were usually a hyperplasia leading to further disease of the acessory sinuses. He attributed the hyperesthesia of the nasal mucosa, in part, to the primary condition causing the asthma and, in part, to the subsequent pathology in the

180. Rackemann, F. M.: Asthma, Hay-Fever, and Allied Conditions, M. Clinics N. America **3**:1065 (Jan.) 1920.

181. Alexander, H. L., and Paddock, R.: Bronchial Asthma; Response to Philocarpin and Epinephrin, Arch. Int. Med. **27**:184 (Feb. 15) 1921.

182. Shambaugh, G. E.: The Nasal Cavities and Asthma, Illinois M. J. **39**: 10 (Jan.) 1921.

183. Jesberg, S.: A Study of Nasal Conditions Occurring in Bronchial Asthma, California State J. M. **19**:33 (Jan.) 1921.

nose. This nasal pathology tends to maintain the asthma even after the primary cause has been disposed of, and accordingly he felt that the rhinologist should work in coöperation with the internist, eliminating the nasal factor of the disease in the interest of permanent cure of these sufferers.

In advocating the early removal of enlarged adenoids in infants, Freeman [184] stated that adenoid obstruction in infancy leads to a number of reflex mainifestations which are not usually recognized as having any relation to adenoid obstruction. Among these he included failure to gain in weight, restlessness, convulsions, eczema and asthma.

Rackemann [185] stated that in treating asthma, one must recognize that it is a symptom complex which depends on one or the other of two great groups of causes. Either the cause is a foreign protein which exerts its influence from outside the body, i. e., an extrinsic cause, or it produces its effects from some focus usually of bacterial growth and action within the body, an intrinsic cause. The treatment of this last group consists either in eradicating the focus by surgical means, if possible, or in the use of bacterial vaccines made preferably from the same strains which are causing the focus of infection, or finally by surgery and vaccination together. Inasmuch as the search for a focus is usually futile, it is assumed that a chronic infection of the bronchi is responsible for the asthma and vaccines are prepared from the sputum bacteria.

In discussing this vaccine treatment of intrinsic asthma, Rackemann believed that the following line of argument is permissable, granting that the results of the treatment are substantial and that the importance of a positive skin test as a prerequisite to successful treatment is not overestimated. It is known that in horse asthma and ragweed pollen asthma, the symptoms depend on an exquisite sensitiveness to the particular foreign protein. Inasmuch as circulating antibodies are not formed we assume that this condition of sensitiveness is cellular. The specific protein will produce a positive skin test and repeated injections will cause relief of symptoms. This treatment is specific. In intrinsic asthma, vaccines likewise produce a positive skin test and as treatment with them is successful only in case the test is positive, their action is specific. By analogy, therefore, we may assume that asthma due to bacteria depends probably on a condition of specific cellular sensitiveness either to the bacteria themselves or to the product of their action in the organism.

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184. Freeman, R. G.: The Results of the Presence of Adenoids in Infancy, New York State J. M. **21**:50 (Feb.) 1921.

185. Rackemann, F. M.: The Relation of Sputum Bacteria to Asthma, J. Immunol. **5**:373 (July) 1920.

In his summary, D. W. C. Jones [186] stated that in the treatment of asthma, one has to consider an irritable center, the hysterical influence of that center, infections of the bronchi and parts of the lungs below them, more especially with specific bacteria whose toxins induce the paroxysms, abnormalities of the respiratory tract superior to the bronchi, and irritation of viscera outside the respiratory tract altogether.

Caulfield [176] gave in detail his technic for the intracutaneous tests, and stated that he felt that at present we have no satisfactory evidence that the injudicious use of a polyvalent solution may not sensitize a patient against other pollens than those to which he was originally sensitive. Gottlieb [187] described the technic of specific therapy, and Mackenzie [188] described the method of desensitization necessary when it is desired to give diphtheria or other antitoxin or pneumococcus Type I serum to "horse" asthmatics or victims of an allergic rhinitis.

Hutcheson and Budd [189] treated eighty-one cases of bronchial asthma with vaccines. About 75 per cent. showed definite improvement, and of those who were considered unimproved, none had had a second series of injections.

As for the drug treatment of asthma, Marfan [190] noted that small doses of potassium iodid, kept up for months or years, had proved useful to ward off the tendency, but for the attacks themselves subcutaneous injections of epinephrin once or twice a day had been effectual. But epinephrin loses its relieving effects on asthma patients after repeated doses, according to Gottlieb,[187] and probably also is not without deleterious effects through its constant elevation of the blood pressure. Gottlieb also described the preventive, climatic and drug treatment of asthma, and noted the surprising relief obtained by inhaling the fumes from a smouldering powder made from nine parts of stramonium leaves and one part of potassium nitrate. In two boys in whom pulmonary emphysema was considered responsible for the attacks of asthma, LeClerv [191] used tartar emetic first and then injections of from 2 to 4 cg. of emetin daily for five days and another series of injections after an interval of from five to ten days. There was a gradual disappearance of the symptoms, and four years later

186. Jones, D. W. C.: The Factors Concerned in Asthma, and Their Treatment, Lancet **1**:484 (Feb. 28) 1920.

187. Gottlieb, M. J.: The Treatment of Bronchial Asthma, J. A. M. A. **74**: 931 (April 3) 1920.

188. Mackenzie, G. M.: Serum Desensitization, J. A. M. A. **76**:1563 (June 4) 1921.

189. Hutcheson, J. M., and Budd, S. W.: The Treatment of Bronchial Asthma with Vaccines, Virginia M. Monthly **46**:281 (Feb.) 1920.

190. Marfan, A. B.: Asthma in Infants, Presse méd. **28**:481 (July 17) 1920.

191. LeClerc, R.: Emphysema of Asthmatic Type, and Emetine Chlorhydrate, Bull. et mém. Soc. méd. d. hôp. de Par. **44**:802 (June 11) 1920.

one of the boys was found to be still free from the symptoms and signs of asthma.

Hay-Fever.—Walker [192] whose writings on this subject are among the most authoritative today, discussed in detail the various causes of seasonal hay-fever, and the methods of determining these causes and the degree of sensitization. He also described the methods of immunization.

Rackemann [178] described his method of treatment for ragweed hay-fever and noted that in ninety-one patients, eight were entirely freed of their symptoms and fifty-seven were considerably relieved. Of the remaining twenty-six patients, fourteen showed some slight relief while twelve had absolutely no relief or were even worse.

In a discussion of "group reactions" in hay-fever, Caulfield [176] stated that from the entire absence of correlation between different pollens to which different patients have been shown to be sensitive, the evidence at present available points strongly against group reaction and suggests on the contrary that sensitization for one pollen is entirely specific for that pollen only. But after a successful desensitization with one pollen, any subsequent desensitization against a different pollen was more easily and rapidly accomplished.

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192. Walker, I. C.: The Causes and Treatment of Seasonal Hay-Fever, M. Clinics N. America **4**:1673 (May) 1921.